STUDIES UPON THE CEREBRAL CORTEX IN THE NORMAL HUMAN BRAIN AND IN DEMENTIA PARALYTICA.

By G. Alfred Lawrence, Ph.D., of New York.

INSTRUCTOR IN DISEASES OF THE MIND AND NERVOUS SYSTEM, NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL.

(*Continued from page* 716.)

Occipital Region.—Coming to the posterior pole of the external cortex, the typical structure of the occipital lobe is represented by Plate VIII, Fig. 24, a section magnified 14 diameters from a block taken from the point indicated by the figure 8, Plate I, Fig. 1. The section is 6 2-3 microns in thickness, is 6 mm. in width at the widest portion, and 7 mm. in length, stained with methylene violet, fixed in Van Gehuchten's fluid, other technique as previously described. This convolution is seen to be quite different in shape from the two previously described of the temporal and parietal regions, having a broader base and narrower rounded vertex. The cortex is seen to be thickest on the lateral aspect *b*, thinner on the opposite lateral aspect *c*, and thinnest at the vertex in the vicinity of *a;* the central white medullary substance being reduced to a minimum. The outer layer varies in thickness, being thickest at *c*. Above this it is broken away for a short distance, is quite thin at the vertex, and becomes somewhat thicker on the lateral aspect *b*. Above *b* the section is seen to be cracked, an artefact resulting from its fixation upon the slide, also at *c* numerous small breaks are noticed, due to the microtome knife. Opposite *a*, and enclosed in ink lines, is the segment of this section, represented in Plate IX, Fig. 25, under a magnification of 100 diameters. The radial arrangement of the cells is well made out at the vertex, but not quite so readily seen on the lateral aspects of the gyrus here, but under a higher magnification can be distinctly made out. About the middle of the second layer, especially at the vertex, some very large pyramidal cells are to be seen singly or in groups, and approaching the Betz cells in type in some cases. The third or lower layer presents nothing unusual, and disappears below into the white medullary substance of the interior of the gyrus. Plate IX, Fig. 25, is a photomicrograph of the segment *a*, enclosed in ink lines in Plate VIII, Fig. 24, at a magnification of 100 diameters. Here the cortex is found thinner than in any of the preceding plates, measuring scarce 2 mm. in thickness. The first layer averages only .15 mm. in thickness, and in structure and arrangement of the cells is similar to this layer in the preceding plates. The second layer measures 1.15 mm. in thickness, containing small pyramidal cells above and quite closely packed together, but increasing in size below and being somewhat more scattered. About the middle of this layer a number of large cells are seen, many singly, but some arranged in groups in places.

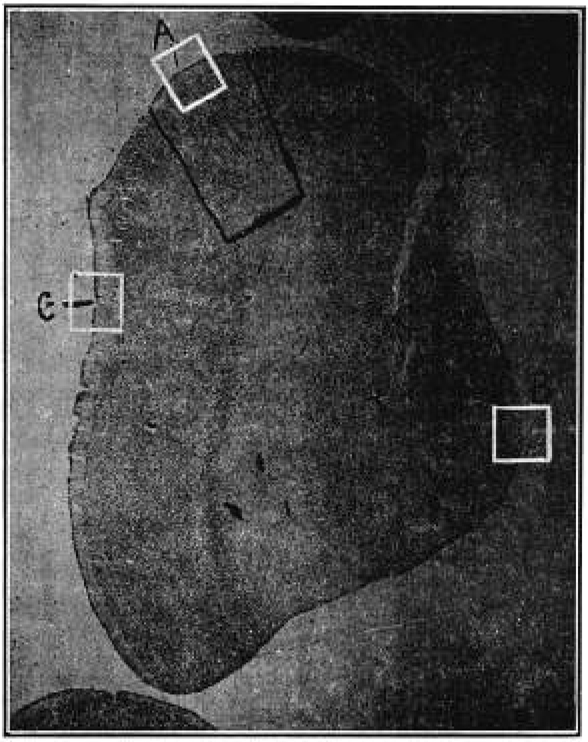

Plate VIII, Fig. 24.

Some of these are even larger than those found in the parietal convolution, and are intermediate in size between the Betz or giant pyramidal cells and the large pyramidal cells. These latter are not very numerous in this region, the small pyramidal cells making up by far the greatest part of the cellular elements of this layer. Below the middle of this layer is to be found a region, at *a*, almost exclusively made up of small pyramidal cells about .25 mm. in width. Between this and the lower border large pyramidal cells are again found intermingled with the smaller. The third or spindle cell layer is here .70 mm. in thickness, containing larger and smaller spindle and irregularly polygonal cells, the lower border being gradually lost in the white medullary substance below. The nerve cells are found quite numerous and closely aggregated in this region, as counts by the same method and manner as in all previous sections, give here an average of 164 nerve cells to the square millimeter of surface of the section, and 199 neuroglia cells, the section being 6 2-3 microns in thickness and stained with methylene violet. The cells are thus seen to be more numerous than in any other region of the external surface of the hemisphere, with the exception of the posterior central convolution. The fact of the greater number of the pyramidal cells being small, permits of their closer aggregation, and no doubt is an important factor in the result of the nerve cell counts. The number of neuroglia cells averages higher than in any other region posterior to the fissure of Rolando, but they are less in number than in the anterior central convolution.

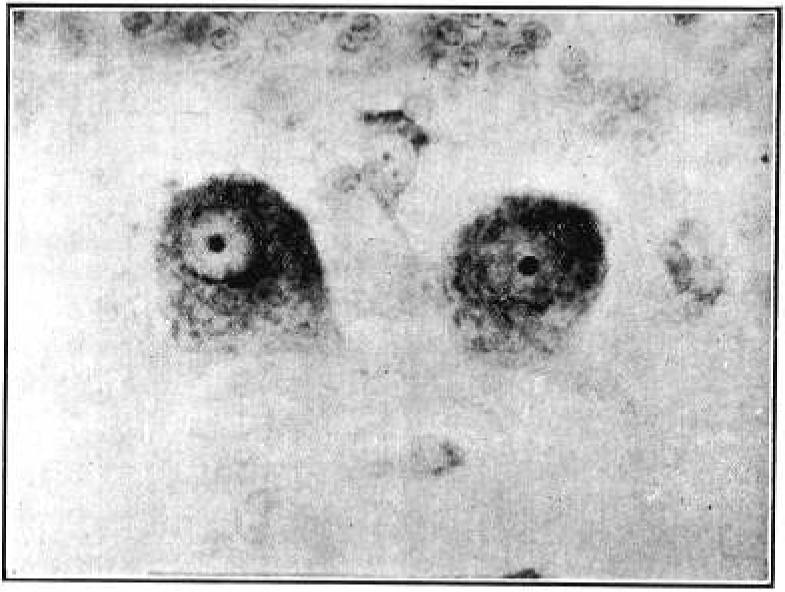

Plate IX, Fig. 27.

This includes the plates of the external surface of the cortex, but for the purpose of comparison, several plates will be introduced from other parts of the central nervous system. The first of these is a photomicrograph, Plate IX, Fig. 26, of several large pyramidal cells from the layer of large pyramidal cells of the hippocampus major or cornu ammonis; between the alveus, representing the white medullary substance of the ordinary gyrus, and the stratum radiatum containing the apical dendrite processes of these hippocampal pyramidal cells. This plate and the two following are not presented as a basis of comparison with similar regions of the pathological brain subsequently to be described, but to give an idea of the appearance of these cells in a normal brain as seen in a photomicograph of a Nissl preparation magnified 1,400 diameters, as distinct types in Nissl's classification.

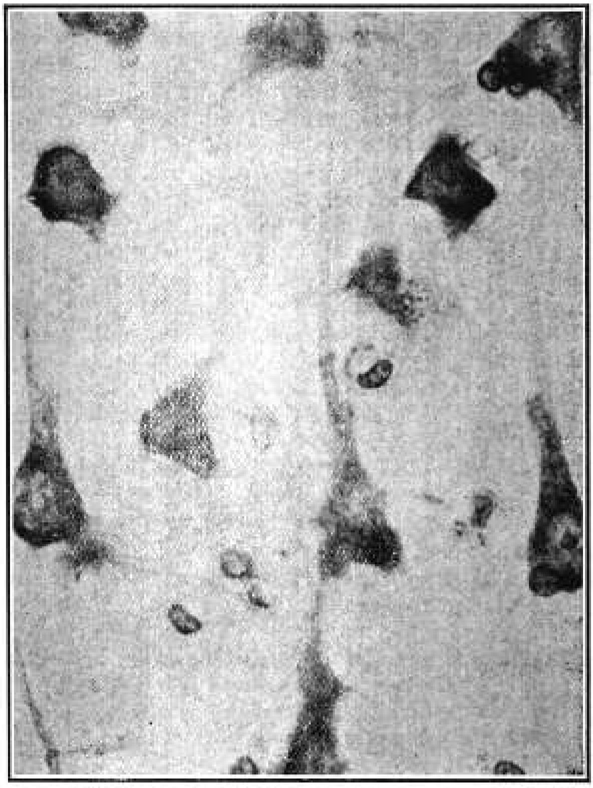

Plate IX, Fig. 26.

These large cells of the cornu ammonis are given as one of the four types of Group II of the stichochrome nerve cells in his classification; the other three types being (1) the nerve cells of the motor nuclei, (2) certain cells of the cerebral cortex, and (3) certain cells of the spinal ganglia. In shape these cells approach the larger pyramidal cells of the external surface of the cortex, second layer, but are somewhat more slender, of a narrow pyramidal shape, have fewer basal dendritic processes, and a long, somewhat slender, apical dendritic process. The chromatic substance here is made up of very small granules fusing into larger and smaller masses in places, so that in the photomicrograph it is difficult to differentiate and determine their arrangement accurately. In some of the cells, as in the cell to the extreme right of the plate, and partially out of the field, the rounded and linear granules above the nucleus, and extending into the apical process, are seen to have a general parallel arrangement. The nuclei of these cells are large, and contain a large, well marked nucleolus and a more or less irregular chromatic network. As this section was stained with methylene violet, numerous neuroglia cells are distinctly seen scattered among the pyramidal nerve cells.

From the cerebellar cortex a photomicrograph was taken of two Purkinje cells, magnified 1,400 diameters, and shown in Plate IX, Fig. 27. The section from which this photomicrograph was taken was situated on the external surface of the left hemisphere, cut transversely to the horizontal axis of the same, fixed in alcohol 95 per cent, stained with methylene blue; other technique similar to that of previously described plates. The section is 10 microns in thickness. These Purkinje cells were given by Nissl as typical examples of what he formerly described as Group II, arkyostichochrome nerve cells of the somatochrome class, in which was presented a striated appearance, with a network-like structure, united in a most intricate manner, thus having characteristics of both the arkychrome and the stichochrome cells. He now classifies them as one of the types of Group I, the arkyochrome nerve cells. In the Purkinje cell, to the right, the base of each of the two large dendritic processes is seen, one going off to the right, the other to the left, subsequently to divide and subdivide in the internal layer, not shown in the plate. The Purkinje cell to the left shows only one of these processes in this plane, that going off to the left which divides in the same manner as above described for the other cell. The large rounded nucleus, with its centrally placed nucleolus, is fairly well shown in the cell to the right, and contains a fine network of chromatic substance. The chromatic substance of the body of the cell is made up of larger and smaller irregularly-rounded chromophilic bodies, arranged in an indefinite network extending up into the base of the dendritic processes. A nuclear cap is seen above the nucleus of the Purkinje cell on the right. The closely-packed fine granular cells of the granular layer of the cerebellum are seen just below these two Purkinje cells, and are included in the class of cytochrome nerve cells in Nissl's classification. They contain a nucleus almost filling the cell body, and which is surrounded by only a very narrow rim of chromatic substance. Within the nucleus is a nucleolus, and in some of these nuclei several irregularly-arranged chromatic granules are also seen. Between the Purkinje cells is a small nerve cell with rounded body and an apical dendritic process. It contains a nucleus, nucleolus, and some chromophilic granules irregularly arranged in the cell-body.

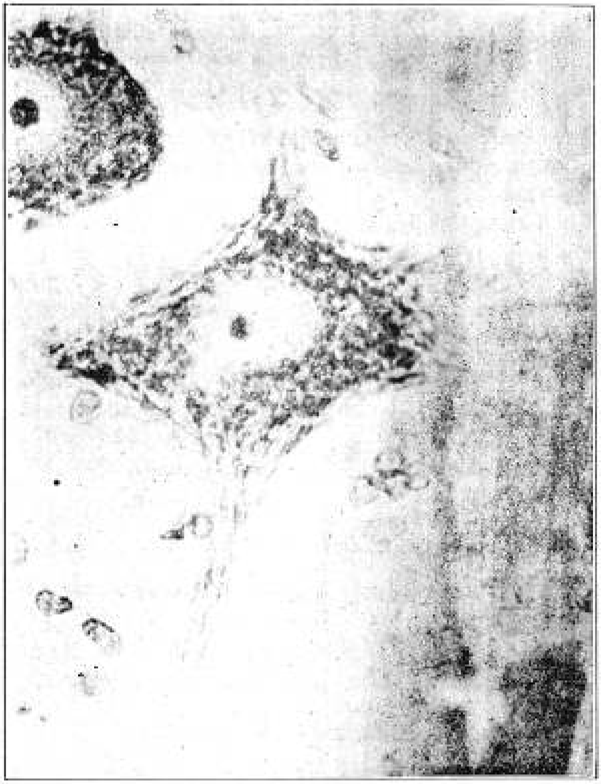

Plate X, Fig. 28.

The last photomicrograph in the series of the normal histological material is that shown in Plate X, Fig. 28, of a typical multipolar ganglion cell from the anterior horn of the lumbar enlargement of the spinal cord, under a magnification of 1,400 diameters. The segment of cord from which the section was taken was fixed in Van Gehuchten's fluid; this section is 6 2-3 microns in thickness and stained with methylene violet. This cell is, according to Nissl's classification, an arkyochrome nerve cell, Group I, of the somatochrome class, the chromophilic bodies being arranged more in the form of a network than in a parallel arrangement in the cell-body, though within the dendritic processes these bodies are more or less distinctly parallel in arrangement. The cell-body is irregularly polygonal in outline, with five large dendritic processes going off in different directions, and containing at the base, and for a considerable distance, linear-shaped chromophilic bodies, arranged in a more or less parallel manner and spreading out and connected with the cell-body network. This latter is made up of irregularly-rounded and elongated chromophilic bodies, arranged in an irregular network. The nucleus is large, rounded, slightly eccentric in situation, and contains a large rounded nucleolus and a pale indefinite network of chromatic substance. Numerous neuroglia cells are seen scattered about, singly or in groups, in the immediate vicinity of this cell. Part of another large ganglion cell is seen at the upper portion of the plate, on the left.

This concludes the very brief discussion of the cortex of the normal brain, in which an endeavor has been made to present typical sections of the main divisions of the external surface of the cerebral hemisphere by means of photomicrography, upon which the greatest care was employed, in order to give an accurate idea of the usual appearance to be seen under the microscope in the study of such sections in contradistinction to the common diagrammatic figures that one usually associates with such work, and which do not show the actual arrangement and structure, but rather the ideal or embodyment in one figure of what is to be found in parts of many. The writer, on the other hand, does not wish to be understood as not favoring diagrammatic or schematic figures in work of this kind, as he regards them as highly important and a valuable accessory to photomicrography and accurate drawings in the proper conception of the intricate structure and arrangement of the various portions of the nervous system as well as other systems. That there are minor variations from these plates in the different regions has been repeatedly stated, but the variation is only a minor one, and does not depart sufficiently from the type to be considered as more than a modification. Furthermore, in going over the various plates from the different regions it will be seen that there is a general uniformity of arrangement and structure of the cells, and that one region does not vary to any great extent from that of any other region. This is well illustrated by comparing the plates from the frontal region with those of the temporal region, in which it would be difficult to determine the one from the other. The Betz cells in parts of the motor cortex are a conspicuous modification, but when we consider that only a small part of the motor area contains these cells, and again that these cells, though large, represent but a minute fraction of the total number of cells in the cortex at this point it will be seen their presence makes but a slight modification in the general cortical arrangement as a whole. The pyramidal cells intermediate in size between the large pyramidal cells and the Betz cells are of especial significance to the writer as perhaps indicating that, with increased specialization of function, carried on through long periods of time, increased specialization of the structure and size of the cortical cells is going on hand in hand, and that perhaps the so-called Betz cells, now almost entirely limited to certain portions of the central convolutions, some time in the future may be found in all parts of the cortex. Their large size, with resulting large amount of protoplasm in the cell-body and large nucleus, the comparatively enormous amount of chromatic substance, as possibly stored up food products, all point to great capacity for storing up nervous energy to be given out when indicated as powerful efferent impulses, or, on the other hand, the capacity of receiving as equally powerful different impulses. Increased specialization in mental activity may result in greater numbers of nerve cells being set apart and increased in size and capacity for carrying out special functions.

Paretic Brain.—Turning now to Brain B, the case of dementia paralytica, from which all the succeeding plates were taken, we see in Plate X, Fig. 29, a photograph of the left hemisphere of the brain, natural size. The macroscopic appearance at first sight would seem to indicate that there was marked atrophy and shrinkage in parts of several convolutions, especially the anterior central and frontal convolutions; but a careful study of the sections taken from these regions shows this not to be altogether the case, or at least only to a slight degree. As any one who has studied brain topography to any extent well knows, there is much variation, not only in the shape and arrangement of any given convolution, but also in its size, so that great care should be observed in not mistaking such normal variation for atrophy. A study of the various plates shown here under a magnification of 14 diameters, containing the entire cross section from the several convolutions in the brain and comparing them to the preceding brain will make this point clear. Here and there a considerable quantity of the cortex has been torn away with the pia mater, whereas in many places small depressions are seen in which only a very small portion of the superficial layer of the cortex has been torn away. The convolutions are here well marked and the sulci very deep, so that there is a large area of cortical surface. The sulci in the middle portion of the hemisphere are widely open, owing to the support being placed only in the middle of the median surface of the hemisphere, so that the weight of the poles, anterior and posterior, caused these latter to become depressed, resulting in this conspicuous widening of the central sulci. The posterior pole of the brain—the occipital lobe—is practically normal macroscopically, and it will be seen later also microscopically, there being none or but very slight pathological changes in the cortex in that region. This photograph of the brain was taken before any blocks were removed, it having been previously fixed in 95 per cent alcohol. As each block was removed the exact location was noted and indicated in the photograph by the letters of the alphabet, and the place from which the block was taken enclosed in ink lines.

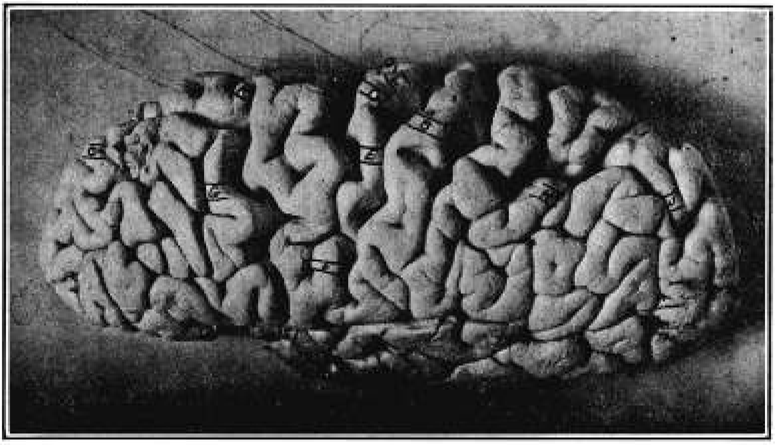

Plate X, Fig. 29.

Frontal Convolution.—This portion of the cortex is represented by the block K, taken from the external surface of the first frontal convolution in its middle third, the exact location being seen in Plate X, Fig. 29, K. The photomicrograph seen in Plate X, Fig. 30, was taken from a section 10 microns in thickness, and is magnified 14 diameters. The gyrus here is somewhat narrow, and the sulci on either side were quite open and deep, and from the macroscopic appearance one might at first be inclined to think that there was some atrophy of the gyrus; but a detailed study of sections from this region shows that this is not the case. Block K was fixed in 95 per cent alcohol; this section is 1 cm. in length, .63 cm. in width at its widest part, and, as above stated, 10 microns in thickness, being stained with methylene blue; the other technique being the same as for all the other plates. The shape of the section is somewhat that of a truncated pyramid, broader at the base and narrow at the rounded vertex. This mechanical arrangement makes the cortex thicker at the vertex than on the lateral aspects. At *a,* and enclosed in ink lines, is the segment represented in Plate XI, Fig. 31. The first or superficial layer is seen to vary somewhat in thickness, being thicker on the lateral surface below *b,* with another thickened portion below *a,* a third just to the left of the vertex, and finally at the lower part of the left lateral aspect. The second or pyramidal cell layer does not show quite as distinct arrangement of the cells in a radial direction as in the corresponding region of the normal cortex, and there is especially to be noted the numerous portions of minute capillaries of varying size and tortuosity, singly or

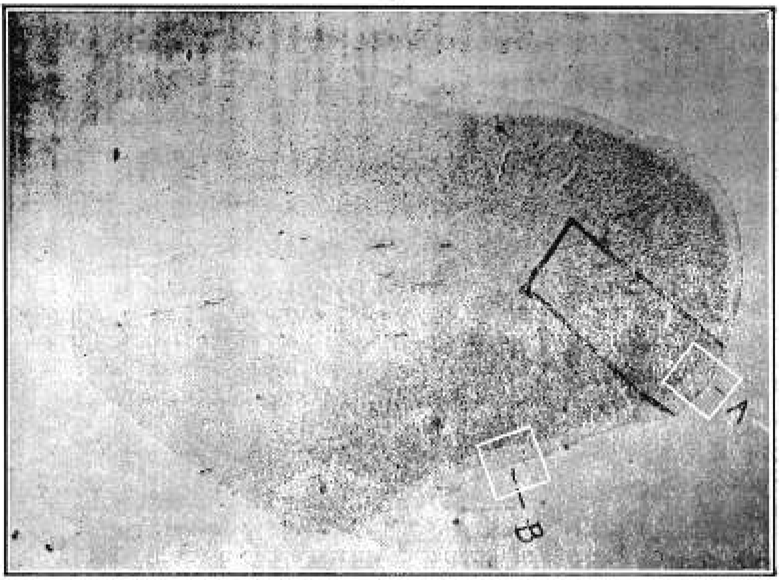

Plate X, Fig. 30.

branched. This second layer passes over into the indistinct third layer, which is lost below in the pyramidal-shaped white medullary center, which also contains numerous capillaries. Plate XI, Fig. 31, is a photomicrograph, magnified 100 diameters, of a segment corresponding in position to *a* of a section adjacent to and from the same block as that shown in Plate X, Fig. 30. The section is 6 2-3 microns in thickness, and of the same length and breadth as that shown in the preceding plate. Decolorization has been carried on to a considerable extent, about to the same degree as in Plate II, Fig. 3, and thus causing the plate to appear rather pale. Additional causes are the paucity of large pyramidal cells in the second layer, and the shrunken condition of many of the cells, as well as other pathological alterations. The upper layer averages .20 mm. in thickness, and contains for the most part scattered neuroglia cells. The second or pyramidal-cell layer is 1.80 mm. in thickness. Here is to be found a very similar arrangement of the cells to that in the corresponding region of the normal brain A. In the upper portion are to be seen the small pyramidal cells in considerable numbers, just below the superficial layer. Then they become more scattered, with a tendency to an arrangement into larger and smaller irregular groups, the cells becoming larger in the deeper portions. A little below the middle of this layer is found a narrow strip at *a,* where the small pyramids predominate almost to the entire exclusion of the larger ones, which latter, however, are seen above and below. Below this again are to be seen the larger pyramids, which finally give way to the irregular and spindle cells of the third layer. The nerve cells themselves show various changes. Many of them appear to be atrophied or shrunken, this process varying in degree in different cells. This in many cases has resulted in the formation of larger or smaller pericellular spaces as seen about many of these cells, as at P in this plate and in Fig. P of the text, for instance. Here a large pericellular space completely surrounds the cell. The basal dendrites are represented by only one small shrunken process given off at the left and extending but a short distance. The body of the cell is shrunken and irregular in contour. A large mass of yellowish pigment is seen at the base to the right. A small amount of finely granular chromophilic substance is found about and above the nucleus. The nucleus itself is displaced downward into the base of the cell-body, to the extreme left. It is small, irregular in outline, and contains a well defined nucleolus but no chromatic substance. The apical process is shrunken and irregular in direction, and contains traces of chromophilic substance in places. The chromatic substance in the large majority of these cells has become diffused and decreased in amount in variable degrees, so that a large number of the cells present the appearance of chromatolysis up to almost complete disappearance of chromatin in some of them. These latter present a pale, washed-out appearance, as shown by the cell marked Q in this plate and seen enlarged in Fig. Q, where only a small amount of chromatin is found in the apical process and a slight amount of pigment in the lower part of the base. Some cells show loss of chromatin only about the nucleus, and are spoken of as instances of central chromatolysis. Others have a disappearance of chromatin at the periphery of the cell-body only, and this condition is known as peripheral chromatolysis. The nuclei of many of these cells are found frequently displaced to one side, crowded into the base of a dendritic process, near the base of the cell-body, or near the base, or up into the proximal portion of the apical process. Many of these are irregular in shape and diminished in size. Quite a large proportion of the larger pyramidal cells contain light yellowish pigment in variable quantity and usually at the base of the cell, often extending into the base of a dendritic process. The cell P, above described, in addition to the pericellular space, demonstrates these last two points, the nucleus being crowded into the base of the dendritic process given off on the left and a considerable deposit of pigment being found at the base and extending into the right dendritic process. The cells containing this pigment are marked with a cross, adjacent to them, in this plate. It will be seen that they are to be found mostly in the middle and lower portion of this layer, and also some few scattered irregular-shaped cells in the third layer. The dendritic processes in many of these cells end abruptly beyond their base, and in but few cases can they be traced to any great distance from the cell-body. The apical process shares in this general atrophy, and often is curved and irregular in direction, instead of presenting a regular straight course towards the periphery of the cortex. In some cells the nucleus is difficult to distinguish, the limiting membrane being indeterminable and the nucleolus appearing to be in the midst and surrounded by only the cell-body, and usually in an eccentric position. Numerous blood vessels are here to be seen, all with thickened walls and pursuing a tortuous course. Large perivascular spaces are also seen about many of these blood vessels, as at *d*, for instance. The third, or spindle or irregular cell layer is here .90 mm. in thickness, and is made up of irregular and spindle cells, some of the former, as some of the cells of the second layer, contain pigmentary deposits. Here also the chromatin is found in diminished quantity, and various stages of chromatolysis are seen. The nucleus is diminished in size in many cases and does not appear to be as prominent a factor as in the normal cells of this region. The cells as a whole appear smaller in size and more or less atrophied, containing less protoplasm in the cell-body as well as a diminished amount of chromatin. The blood vessels are here also found to have thickened walls, and are tortuous in direction. At *e* is seen one of these vessels, with thickened walls and surrounded by a large perivascular space. The entire thickness of the cortex at this point is found to be 2.90 mm.; almost the same as in the corresponding region in Brain A, as seen in Plate II, Fig. 3. Counts were made of the nerve and neuroglia cells in various parts of this section in the same manner as in the previous sections, and in eight different fields of 36 sq. mm. each of the ocular net-micrometer from various portions of the two lower layers for the nerve cell counts, and in all three layers for the neuroglia cell counts. There was found to be an average of 100 nerve cells and 56.90 neuroglia cells to each square millimeter of surface of this section. The small number of neuroglia cells being due to the methylene blue stain employed and differentiation carried on to a considerable degree in a section 6 2-3 microns in thickness. In the section shown in Plate X, Fig. 30, 10 microns in thickness, and more deeply stained, the number of nerve cells is not quite so great, whereas the number of neuroglia cells is almost six times as great, although the two sections are quite near together and from the same block. This is due to the neuroglia cells in Plate XI, Fig. 31, being almost completely decolorized in the greater differentiation, whereas the cells, although paler, yet were not decolorized, and can all be made out. The same method of using the ocular net-micrometer was employed here as in all the other plates, and counts were made from eight different fields of thirty-six squares each from different parts of the second and third layers of this section, and the average number of nerve cells was found to be 82.91 to the square millimeter of surface of the section, as compared to 100 for the same area in Plate XI, Fig. 31, so that there are on an average less nerve cells in this section, 10 microns in thickness, than in the section from which Plate XI, Fig. 31 was taken, which was but 6 2-3 microns in thickness, the same stain being used in both cases. The nerve cells, however, are more deeply stained in this latter section, and appear more distinct, and there are also more large cells. The neuroglia cells in eight different fields of thirty-six squares each from various parts of the three cortical layers average 303 to the square millimeter of surface of the section, as contrasted to 56.90 to the square millimeter in Plate XI, Fig. 31. Here increased thickness makes a difference in favor of this plate, and in addition to that the deeper stain with less decolorization cause all the neuroglia cells to appear more prominent. As stated before it was found that sections from 6 2-3 to 10 microns in thickness contain all the nerve cells to be seen in one plane. As the neuroglia cells are much smaller in diameter and often arranged in dense clusters, there may be a greater number in a section 10 microns in thickness than in one 6 2-3 microns in thickness. (See Table II.)

Central Region.—Turning to the region posterior to the one just discussed, we come to the central region, or motor area, made up of the anterior and posterior central convolutions. Typical of the anterior central convolution in its upper portion is the section represented in Plate XI, Fig. 32, under a magnification of 14 diameters. The exact location of the block from which this section was taken is indicated by the letter D in Plate X, Fig. 29. The wide separation of the convolutions from one another, with resulting gaping sulci, is especially marked in this region. As previously mentioned, this is largely due to mechanical agencies, a central support permitting the opposite poles, owing to their weight, to become depressed and force open the sulci in this region during the process of hardening or fixation. In the removal of the pia mater, small portions of the adhering cortex have been removed in places. This is seen just below the letter O, and in many places in the convolutions both anterior and posterior to this. By referring back to Plate III, Fig. 7 of the normal brain

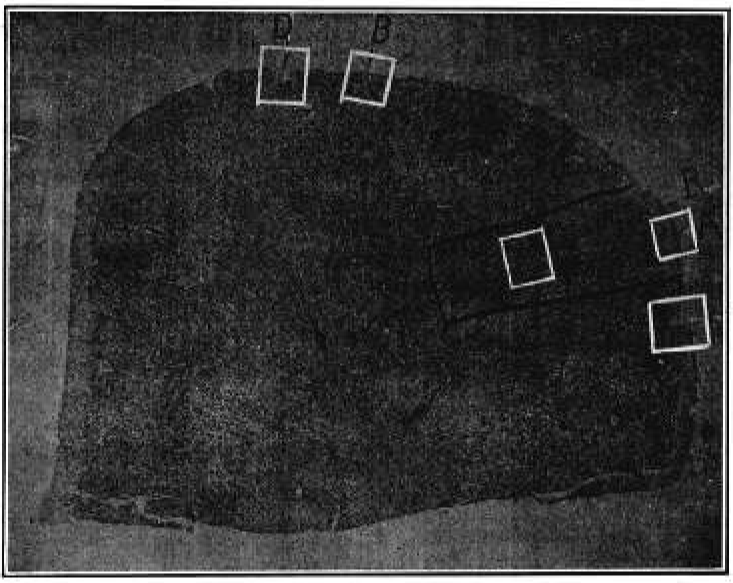

Plate XI, Fig. 32.

it will be seen that this section was taken from approximately the same relative position of the convolution as that seen in Plate III, Fig. 7, and, furthermore, the two convolutions are quite similar in shape; this convolution being somewhat broader and less rounded at the vertex than that of the normal brain, however. The outer cortical layer is here more irregular and torn than in Plate III, Fig. 7, and at the vertex of the convolution at *b* the outer part of the first layer is seen stripped off for some distance. This, of course, is an artefact, the detached part being more adherent to the stripped off pia than to the cortex below. This outer layer furthermore presents a somewhat irregular contour, being broken in places as at *c* and *d*. The layer is thicker opposite *a*, and on the left lateral aspect, than elsewhere. The second or pyramidal cell layer shows the general radial direction of the cells, but not so well marked as in Plate III, Fig. 7. The chief point of interest, however, is almost complete disappearance of the Betz cells, which are seen so prominently in this region in the normal brain in plates of this magnification (14 diameters). In photomicrographs of 100 diameters we will find this disappearance is not complete, and that the cells, although much atrophied and pale, so as to scarcely appear under the lower power, are much more apparent here, and are seen in all stages of dissolution. In this plate only scattered Betz cells are seen singly or in small groups at wide intervals, and these few are small, shrunken and, for the most part, pale. Fig. R is a drawing of the large Betz cell marked R in this plate. The nucleus is quite centrally situated, with a large distinct nucleolus and some faint chromatic substance. Some few chromophilic bodies are seen interspersed among the finely granular chromatic substance. The cell processes are pale, irregular, and soon terminate at a short distance from the cell-body. No pigment is found in this cell. Figs. S and T show two other near-by cells, the former containing an eccentric nucleus, irregular, shrunken cell-body, with some pigment at the left of the nucleus. The processes being irregular and short. The cell in Fig. T is much shrunken and distorted, the nucleus irregular, a small nucleolus, and but little diffuse chromatic substance. There are no basal processes, and the apical process is narrow and irregular in direction. Numerous capillaries are seen with thickened walls, and some with perivascular spaces. The third layer is indistinct, and fades into the white medullary substance, where many large capillaries with thickened walls, tortuous course and perivascular spaces are found. At *a*, and enclosed in ink lines, is the segment of this section, corresponding in position to that seen in Plate XI, Fig. 33. This section is 8 mm. wide, 6.5 mm. long, and 10 microns in thickness, fixed in 95 per cent alcohol, stained with methylene violet, and other technique similar to all the other sections. Plate XI, Fig. 33, is the photomicrograph magnified 100 diameters of a segment corresponding to *a* of Plate XI, Fig. 32, and from a section taken from the same block, and but a short distance from the above. At this point the first or outer layer measures .25 mm. in thickness, whereas in Plate XI, Fig. 32, it would measure at least .40 mm. in thickness. It contains numerous neuroglia cells, with here and there a small pale nerve cell in which is situated a small nucleus surrounded by a mere trace of chromatic substance. Below this is the second or pyramidal cell layer, measuring 1.30 mm. in thickness. In the upper parts the pyramids are seen to be small and quite closely packed together. About the middle of the layer they are seen to be much larger and more scattered. Below this again, at *a*, is seen a region containing for the most part only small pyramids, and this finally merges into the lower portion of this layer, where are seen the large and giant pyramidal cells. These latter, or Betz cells, are seen in irregular groups or "nests," consisting of from one to several (six or more) cells. All of these cells show a diminished amount of chromophilic substance and no distinct granules. Various stages of advanced chromatolysis are seen, from a general diffusion of the chromatic substance to almost complete absence of the same. The cells are for the most part shrunken, the nuclei small and indistinct, displaced in many cases, and the cell processes atrophied and tortuous. Many of these larger cells contain a varying amount of yellowish pigment. Fig. U shows the cell marked U in the plate. No processes are seen, the cell-body is shrunken and contains but a small amount of diffused chromatin, showing no structure and pale in color. The nucleus is small, shrunken and indistinct, with a pale nucleolus. No pigment is to be seen in the cell. To the left of the cell-body is a small pericellular space. Several neuroglia cells are seen in apparent direct contact with the cell-body and others in the pericellular space and the wall of the latter. The cell just below and to the left of this in the plate is similar in regard to the amount of chromatin, is pale, and the nucleus and nucleolus are not visible. Three processes are seen given off at the base, but atrophied and extending for only a short distance. A small pericellular space is seen about this cell also. The cell just below and to the right of this, and marked V in the plate and seen in Fig. V, shows the same grade of chromatolysis. The remnant of a shrunken and atrophied process is seen at the base on the right. The shrunken nucleus, with pale nucleolus, is centrally situated, and below this are found diffused pigmentary deposits. Throughout the cell-body, less in the upper than in the lower part, is scattered pale diffuse chromatic substance, and without any definite arrangement. A narrow pericellular space is seen along the right side of this cell. The general contour and lack of structure are seen in Fig. V. Here, too, neuroglia cells are seen lying upon and in close juxtaposition to the cell-body. Numerous blood vessels with thickened and tortuous walls and perivascular spaces are seen throughout this layer. The third or spindle or irregular cell layer here measures .90 mm. in thickness, and is made up of shrunken spindle and irregular cells, pale, and containing but a small amount of diffuse chromophilic substance. Many of them are surrounded by pericellular spaces of varying size. The letter W indicates one of these spindle cells seen in the drawing, Fig. W. The polar processes are here filamentous, and distorted in direction, the cell-body shrunken and containing but a small amount of diffuse chromatic substance, so that it is pale in color, the nucleus is small and indistinct, and contains a small nucleolus. The cell-body is partially surrounded by a distinct pericellular space, with a neuroglia cell upon the edge at one point. Numerous blood vessels with thickened walls and perivascular spaces are also seen in this layer. The entire depth of the cortex here is 3.05 mm., all three layers being slightly thicker than in Plate III, Fig. 8, of Brain A, the first layer being .05 mm., the second .15

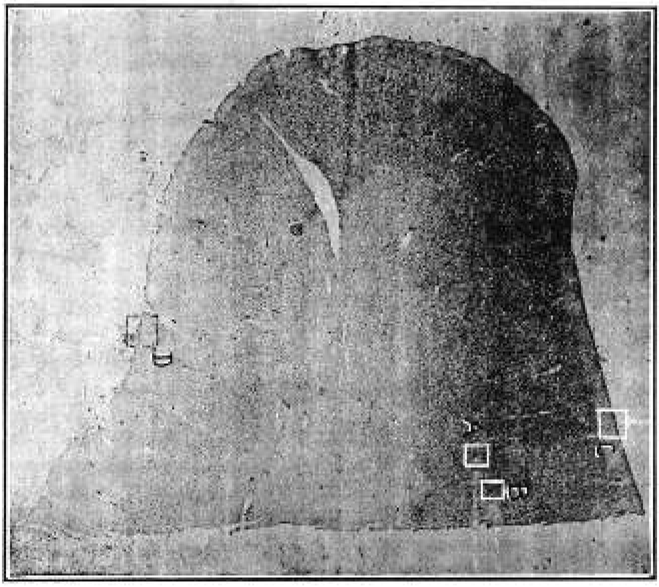

Plate XI, Fig. 34.

mm., and the third .20 mm., thicker than in the latter. As variations of this extent are found in sections of convolutions in close proximity, and even in different parts of the same section in any brain, it seems doubtful to the writer whether we can attach any special significance to such a slight variation, due possibly to mechanical causes, acting in embryonic or even post embryonic life. Counts of the nerve and neuroglia cells here show a decided falling off in number of the former. This section is 6 2-3 microns in thickness and stained with methylene violet. The same method with the ocular net-micrometer was used, counting the nerve cells in eight different fields of thirty-six square millimeters, each in various parts of the second and third cortical layers, and the neuroglia cells in the same number of different fields in all these cortical layers. The average number of nerve cells to each square millimeter of surface of the section was found to be but 39.60, whereas the average number of neuroglia cells to the same area was found to be 204. The number of nerve cells is thus seen to be much diminished as compared to Plate III, Fig. 8, the corresponding region of the normal brain A, where there are an aver-

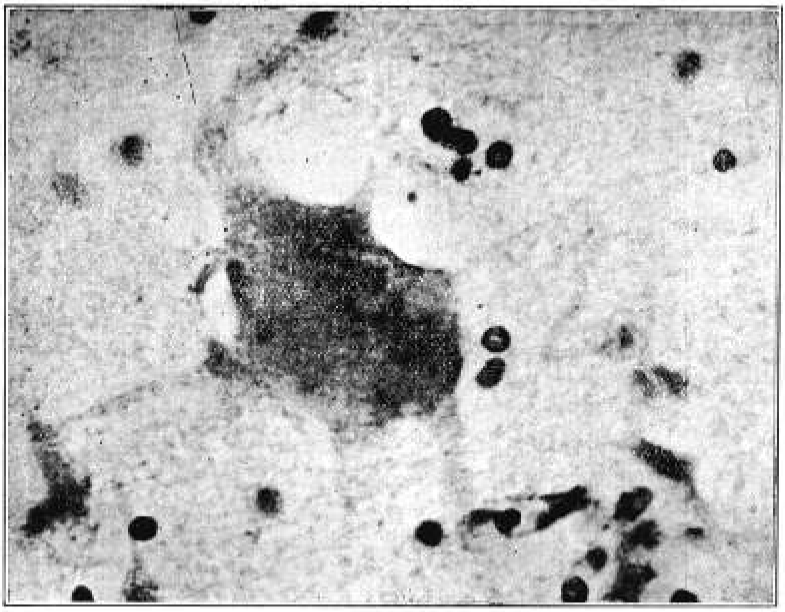

Plate XII, Fig. 35.

age of 95 nerve cells to the square millimeter of surface of the section. The number of neuroglia cells is also less here, being 204 in this plate in comparison to 293 in Plate III, Fig. 8. The latter section is, however, 10 microns in thickness, as compared to 6 2-3 microns for this plate, and as previously noted, owing to the small size and close aggregation of the neuroglia cells, more would be normally found in the thicker section, although this hardly accounts for the great difference, as both were stained in the same manner with methylene violet. Plate XI, Fig. 34, is a photomicrograph, magnified 14 diameters, from a section taken from the point L of the upper portion of the anterior central convolution of Brain B (see Plate X, Fig. 29), and as seen by referring to this latter, is from a more inferior portion of this gyrus

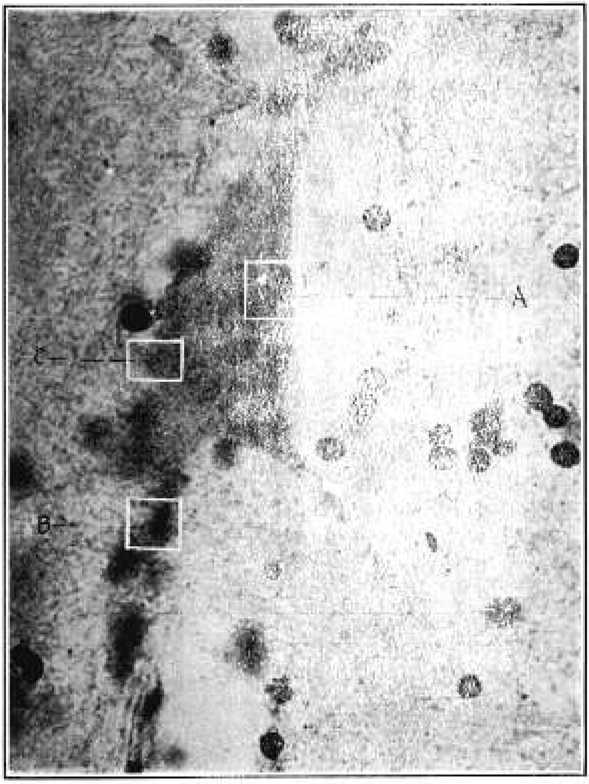

Plate XII, Fig. 36.

than the section represented in Plate XI, Fig. 32. This section was fixed in 95 per cent alcohol, is 6 2-3 microns in thickness, and stained with methylene violet. The first layer is seen to be fairly uniform in thickness at the lower two-thirds, as seen at *c*. Above, and at the vertex, and also along the anterior aspect of the convolution, as at *d*, the surface is more or less torn and irregular, due to carrying away of small fragments with the adherent pia. By referring to Plates XI, Fig. 32, and XIII, Fig. 39, the variations in shape and mechanical arrangement of the convolution in adjacent portions will be noted. In Plate XI, Fig. 32, the vertex is broadly rounded and somewhat flattened. In Plate XIII, Fig. 39, the vertex is more narrow and pointed, while in this plate, intermediate in position between the above two plates the vertex is less pointed. Large perivascular spaces are noted in many places throughout this section, especially marked in the upper portion to the left of the vertex, where but a fragment of the blood vessel is to be seen only at the lowest point of an enormous perivascular space. The radial arrangement of the cells is but poorly shown, the Betz cells seem to have disappeared almost entirely in the second layer, in marked contrast to the plates of the same magnification of Brain A. (Plates III, Fig. 7; IV, Fig. 9, and IV, Fig. 11.) Under a high magnification, however, the remnants of many of these Betz cells can be made out, showing various pathological changes. The other nerve cells also show a wealth of pathological change of varying degree and kind to which the nerve cell is subjected—all grades of chromatolysis, pigmentation, atrophy, and shrinkage of the nerve cells and processes, with larger or smaller pericellular spaces. Numerous capillaries, with thickened walls and perivascular spaces, are seen scattered throughout the various parts of the section. The actual size of this section is 8 mm. wide at the point opposite *d*, 8.5 mm. long, and 6 2-3 microns in thickness. At the points *a* and *b* are seen the Betz cells, shown under a magnification of 1,400 diameters in Plates XII, Fig. 35, and XII, Fig. 36. The former of these is a photomicrograph as stated, under a magnification of 1,400 diameters of the nerve cell, indicated by the letter *a* in Plate XI, Fig. 34. By referring to this latter plate, and then to Plate X, Fig. 29, we can locate almost the exact position of this cell in the cortex of Brain B. The cell-body is seen shrunken and deformed, lying in a pericellular space partially surrounding it. The nucleus is eccentric, being crowded over to the extreme edge of the cell-body on the right side. It is also shrunken and indistinct, but contains a well-marked and prominent nucleolus. The apical process above and to the right appears quite sharply deflected at a point but a short distance from the base, but this is not really the case, as the portion from *a* to the edge of the plate is one of the walls of a blood vessel, the opposite wall not being seen in this plate at all. At the point *a,* this apical dendritic process appears to come in direct contact with this portion of the wall of the blood vessel, and is there lost to view. The other dendritic processes—seven in all—are shrunken, and contain a small amount of diffuse chromatin. Within the cell-body the chromatin is considerable in amount, and quite generally diffused in fine granules throughout the cell-body, lacking any definite structural arrangement. There is a somewhat greater amount at the base to the left and below the nucleus, and also at the upper part of the cell-body. Above and to the left of the nucleus, where the cell-body appears most pale, and extending into the base of the dendritic processes here, is a considerable mass of yellowish pigment. Numerous neuroglia cells are seen in the vicinity of this Betz cell. Plate XII, Fig. 36, is also a photomicrograph, magnified 1,400 diameters, of another of these Betz cells from the point *b* of Plate XI, Fig. 34. Here there is but little diffuse chromatin, confined principally to the base of the dendritic process given off on the right. All the lower part of the cell-body, excepting this portion, contains palely yellow pigment. The nucleus is displaced almost to the extreme edge of the cell-body, and lies just below the two neuroglia cells seen at *a.* The nucleolus, on this account, can not be determined at this plane. On microscopic examination the nucleus is found to be shrunken and indistinct. Numerous neuroglia cells are seen upon and in the immediate vicinity of this cell. The basal dendritic process *b,* which is but faintly seen here, owing to its lying in a somewhat lower plane, has eight neuroglia cells in close apposition to it. The dendritic process on the right can be traced for some distance, is somewhat shrunken, and contains no chromatic substance. Another small dendritic process is given off from the base opposite the point *c,* and being in a lower plane, only its base is seen here. It is colorless, and extends but a short distance from the cell-body. The apical dendritic process contains no chromatin, and as seen, has several neuroglia cells surrounding it a short distance from its base. A large pericellular space almost entirely surrounds the cell, excepting at the base to the left. Plates XII, Fig. 37, and XII, Fig. 38, are photomicrographs of the same magnification (1,400 diameters), taken from an adjacent section of the same block as the two preceding plates, and are also 6 2-3 microns in thickness. This section was prepared in exactly the same way, with the exception that methylene blue was used as the stain instead of methylene violet. This will be at once apparent upon noticing the neuroglia cells, which are here pale and washed out, many to the point of complete decolorization, so as not to be seen at all. The Betz cell in the center of Plate XII, Fig. 37, is seen surrounded by a large pericellular space. All the processes, four in number, including the apical dendritic process, are pale, and terminate but a short distance from the cell-body. The nucleus is eccentrically situated near the wall at the left, is small, and contains a large nucleolus, but no nuclear network. Within the cell-body finely granular chromatic substance is found at the base below and to the right of the nucleus. There is no pigment present. This cell presents an advanced stage of partial chromatolysis. Above and to the right is an almost indeterminable mass, which, under the 1-12 inch oil-immersion objective, appears to be the remnant of a capillary, surrounded by a large perivascular space. Other cells are seen here in various stages of disintegration, surrounded by large pericellular spaces, some containing none or only the remnants of den-

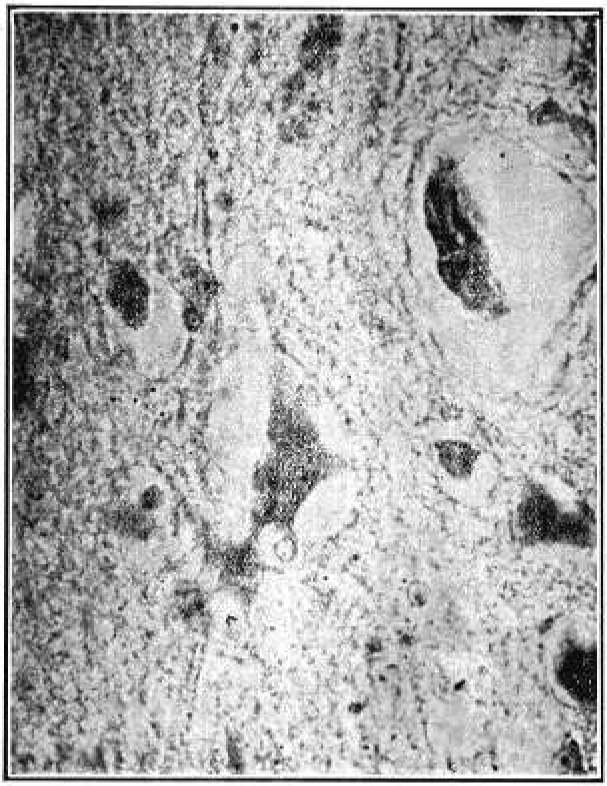

Plate XII, Fig. 37.

dritic processes, indistinct and shrunken nuclei, some distinct nucleoli and others none at all, and all in a more or less advanced state of chromatolysis, with but little of the diffused stained chromatic substance present. The neuroglia cells that are visible at all are pale and poorly stained, while many are almost or completely decolorized. Plate XII, Fig. 38, is a photomicrograph of a Betz cell on the same section and but a short distance from the cells of the preceding plate, and under the same magnification (1,400 diameters). Here there is almost complete chromatolysis, there being but little finely granular, diffuse chromatic substance scattered in the cell-body, slightly more at the base than above the nucleus. The latter is small, rounded, centrally situated, and

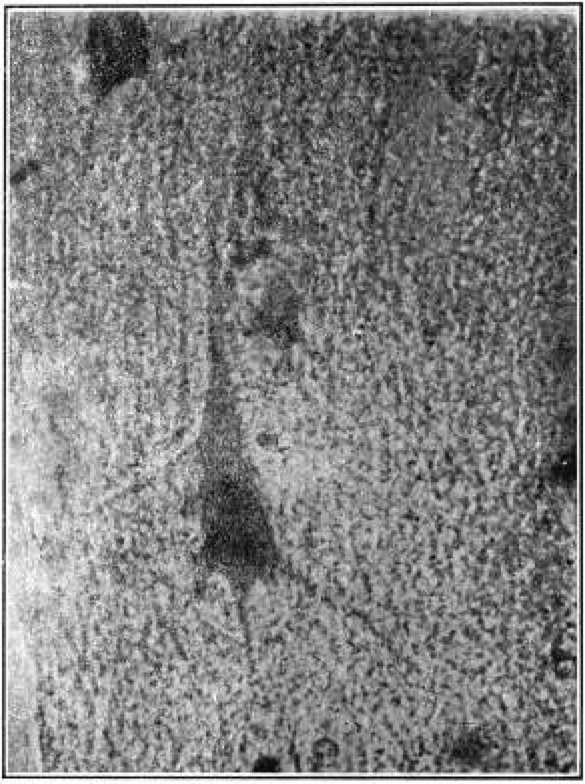

Plate XII, Fig. 38.

contains a large, rounded, distinct nucleolus. The three basal processes are narrow, pale, and terminate at no great distance from the cell-body. The apical process is pale and slender, extending for some little distance before coming to an end. Part of a pale, atrophied cell is seen to the right of the same. The ghosts of several neuroglia cells may be seen here, but most of them are completely decolorized.

Plate XIII, Fig. 39, as will be seen by referring to Plate X, Fig. 29, is from the lower portion of the upper third of the anterior central convolution, from the point marked O, and is magnified 14 diameters. This section, as already mentioned, is found to vary somewhat in shape from that of the preceding sections shown in Plate XI, Fig. 32, and Plate XI, Fig. 34, being narrower and more pointed at the vertex. From the strip marked *a,* and enclosed in ink, the structure and arrangement of the nerve cells were carefully studied, and both nerve and neuroglia cell counts made and will be referred to again later. The irregularity and difference in thickness of the first layer in different parts is to be noted, being especially thick at *b,* where it almost presents the appearance of an artefact, but under a high power no derangement of the structure can be made out. At *a* the layer is seen to

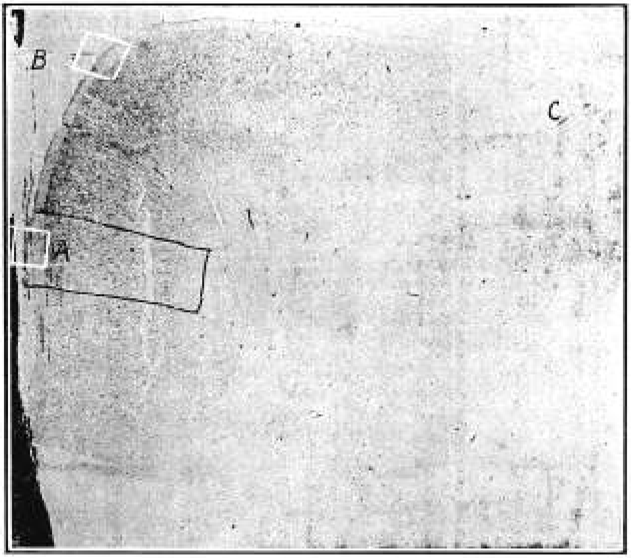

Plate XIII, Fig. 40.

be very thin, owing to some of the surface of the cortex having remained adherent to and been stripped off with the thickened pia mater. Large perivascular spaces are to be especially noticed in the subcortical portion of the section. Here is to be noted the almost entire absence of the Betz or giant pyramidal cells in the lower part of the second layer, although some large pyramidal cells are to be found, they are not, however, so large nor are they arranged in such distinct groups as in the region higher up. Under higher magnification the remnants of some of these Betz cells are seen in various stages of necrosis and disintegration. The cortex lacks the distinct striated appearance seen in the sections of the normal cortex. This layer passes indistinctly into the third or spindle cell layer, which in turn is lost in the white medullary substance below. Numerous capillaries are seen, many with thickened walls and perivascular spaces throughout the section. This section was fixed in 95 per cent alcohol, sectioned 10 microns in thickness, stained with methylene violet, with other technique similar to that of all the previous sections. The actual size of the section is 9 mm. at its greatest width and 13 microns in length. The strip *a* varies from that of Plate XI, Fig. 33, only in the number and arrangement of the cells in the second layer. At this point the three layers are respectively .20 mm., 2.00 mm., and .90 mm. in thickness. The first layer contains some few scattered irregular nerve cells and numerous neuroglia cells. The second layer contains small pyramidal cells above, increasing in size until a little above the middle of the layer is a strip some .30 mm. in width, in which are to be seen large pyramidal cells arranged singly or in irregular groups. Some of these cells almost approach the giant pyramidal cells in size. Many of them show but a slight shrinkage and contain an almost normal amount of chromatic substance. The chromophilic bodies, however, are not as numerous or as large as in the normal brain. Other cells show a complete absence of chromophilic bodies, but contain the chromatic substance diffused throughout the cell in minute particles. Still others are pale, and contain but little chromatic substance. The nuclei are larger, less eccentric, and there is a less degree of atrophy of the cell-body and processes. Below this is a region of small pyramidal cells with only a few scattered larger pyramidal cells merging into the lower part of the layer, where large pyramidal cells are again seen scattered irregularly among the smaller cells. These large pyramidal cells are somewhat smaller than the giant pyramidal or Betz cells seen in the upper part of this convolution. These cells show more advanced pathological changes, in some cases marked atrophy and shrinkage with large pericellular spaces, atrophy of the dendritic processes, eccentricity and shrinkage of the nucleus, pigmentary deposits, complete absence of or but a small amount of diffuse chromatic substance. The third layer presents the same general appearance as in the preceding plate (XI, Fig. 33), with many cells much shrunken and atrophied and little or no chromatic substance within the same, and surrounded by pericellular spaces of varying size. Numerous large and small capillaries are seen scattered throughout this section, with thickened walls and surrounded by larger or smaller perivascular spaces. The entire depth of the cortex here is 3.10 mm., the second layer being slightly thicker than in Plate XI, Fig. 33. The nerve cells were found to average but 36.50 to the square millimeter of surface of the section here; less than in any of the other plates, whereas the neuroglia cells average 289 to the square millimeter of surface of the section, almost as great a num-

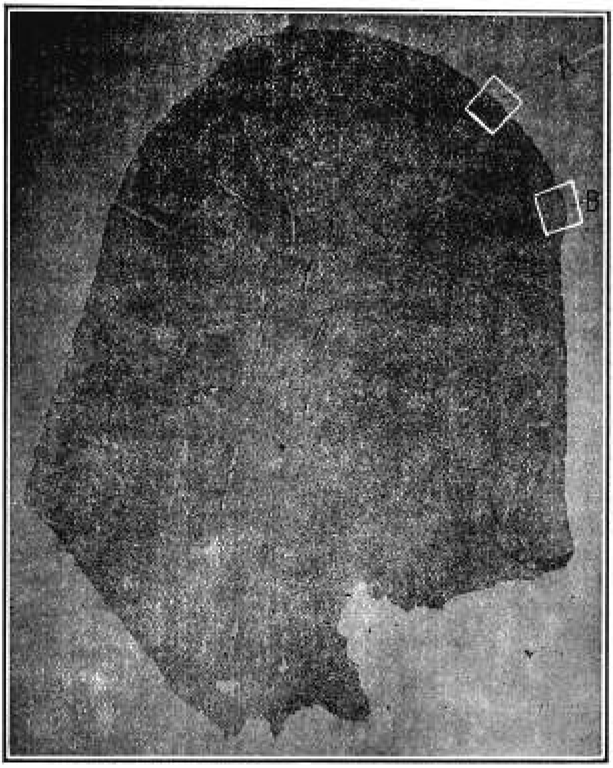

Plate XIII, Fig. 39.

ber as in the previous sections of the same thickness, ten microns, and stained with methylene violet. The most conspicuous difference between this and Plate XI. Fig. 33, higher up in the convolution, is the arrangement of the large pyramidal cells, the absence of the typical Betz cells, and on the whole less advanced pathological changes. Plate XIII, Fig. 40, is a photomicrograph magnified fourteen diameters of a section from the block B of Plate X, Fig. 29, and is thus seen to be situated a little above the middle of the posterior central convolution. This section is 6 2-3 microns in thickness, 8 mm. in length, and 9 mm. in width at the widest point, was fixed in 95% alcohol, stained with methylene blue, and other technique similar to that of all previously described sections. This section at the vertex, especially to the left, shows the striated appearance of cell arrangement very well, but upon the anterior and posterior aspects of the gyrus it is but indistinctly shown. The first layer is fairly uniform in thickness with broken spaces here and there, especially about the entrance of capillaries. This layer is somewhat thicker in certain places than in others. At *a,* for instance, it is thicker than at the vertex. This section has a broad, flattened vertex with considerable cortical area on both the anterior and posterior surfaces. The cortex opposite the angles *c* and *b* is somewhat thicker than elsewhere. This mechanical arrangement admits of a large, broad mass of fibres from various parts of this and the adjacent regions of the brain, leaving from and entering into relations with the cells of this portion of the cortex. The section is broken (an artefact) at the left and numerous capillaries are found scattered throughout all the cortical layers and also the white medullary center. The segment represented in Plate XIII, Fig. 41, was taken from a point corresponding to *a,* but from an adjacent section of the same block, and is magnified 100 diameters. It is from relatively the same position as the segment shown in Plate VII, Fig. 19, the strip *a* of Plate VI, Fig. 18, of the normal brain, but, as will be seen by referring to the latter, the shapes of the two sections are quite different. The distribution and arrangement of the cells in this plate is somewhat different from that in Plate VII, Fig. 19, also. In this latter, as already described, some large pyramidal cells are irregularly distributed in parts of the upper half of the second layer, followed by a narrow region made up almost exclusively of small pyramidal cells to be followed by larger pyramidal cells in the lower portion of this layer. In this plate, however, there are but few of the larger pyramidal cells in the upper portion of the second layer, there being practically only small pyramidal cells in this upper portion with the larger pyramids mostly in the lower portion of this second layer. The cell seen in the lower part near the center (*a,* Plate XIII, Fig. 41), approaches in size to the Betz cell type. The first or superficial layer here contains nothing but capillaries and neuroglia cells and is .25 mm. in thickness. The second or pyramidal cell layer is 1.40 mm. in thickness and shows not only numerous capillaries with irregular and thickened walls, but also the cells in various pathological conditions. Chromatolysis is complete in many of these cells as in the large pyramidal cell marked *a* for instance, where only traces of minute finely powdered chromatin can be seen in some parts of the cell-body. Here also the nucleus is indistinct, with a well marked nucleolus, and the basal processes are much atrophied, terminating but a short distance from the cell-body. A small pericellular space is seen at the base of this cell-body. Many cells show eccentricity of the cell nucleus, shrinkage of the cell-body, various grades of chromatolysis, pigmentation, atrophy, and distortion of the dendritic processes and are surrounded by pericellular spaces. The capillaries are numerous, have thickened and irregular walls, and are surrounded by perivascular spaces of varying size and extent. Numerous neuroglia cells are also interspersed about the cells and capillaries in this layer. The third or spindle cell layer is only partially seen in this plate, and is about .90 mm. in thickness (only upper portion shown in Plate XIII, Fig. 41), and is similar to that in preceding plates of the motor region, and contains for the most part shrunken and irregular spindle and polygonal shaped cells, with numerous neuroglia cells and capillaries interspersed among them. Most of these cells show the various pathological processes mentioned above for the pyramidal cells. The cortex here thus measures 2.55 mm. in thickness, almost the same as for the two upper layers in Plate VII, Fig. 19, but here the third layer is .90 mm. in thickness as compared to .60 mm. in the above mentioned plate of the normal brain. Nerve and neuroglia cell counts were made here with the result that an average of 59.91 nerve cells and 134.37 neuroglia cells were found to the square millimeter of surface of the section as compared to an average of 185.50 nerve cells and 109.20 neuroglia cells for the same area in the strip of cortex represented in Plate VII, Fig. 19, of the corresponding region of the normal brain. Both sections were 6 2-3 microns in thickness and both stained with methylene blue. The difference in nerve cells is very marked, whereas the difference in number of neuroglia cells is not so great, and as the technique was identical throughout in the preparation of the two sections, the marked pathological process shown in this latter, it seems to the writer must be attributed as the cause of this difference to a large extent at least.

Parietal Region.—Plate XIV, Fig. 42, is a photomicrograph magnified fourteen diameters, of the parietal region from the point H. in Plate X, Fig. 29, this being a part of the supra-angular gyrus and from the same relative part of the gyrus as the corresponding plate (VII, Fig. 20) of the normal brain. The section was fixed in 95% alcohol, stained with methylene violet, and treated otherwise as the preceding plates. This section measures 6 mm. in width, 16 mm. in length, and is 6 2-3 microns in thickness. Its shape is long and narrow and quite different from that of Plate VII, Fig. 20. At the vertex of the convolution the first layer has geen cut away with the paraffin in preparing the block for sectioning serially with a Minot microtome, and, of course, this condition is an artefact. The first layer is seen to be fairly uniform in thickness with this exception. In the second layer it is difficult to determine the well marked striated arrangement of the cells, as seen in Plate VII, Fig. 20. Numerous perivascular and pericellular spaces are seen with or without the capil-

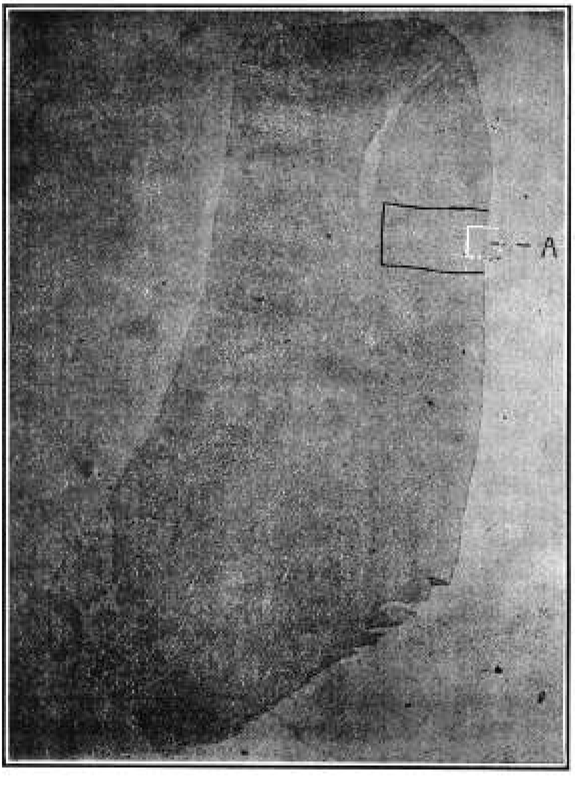

Plate XIV, Fig. 42.

laries or cells, as the case may be. The third layer is indistinct and fades away into the white medullary center which also contains many pericellular and perivascular spaces. No doubt the fixation in 95% alcohol has produced some shrinkage, but by no means all, as the plates of the occipital convolution just posterior to this show a much less degree of shrinkage than is here present and not only every block taken from this brain was fixed in exactly the same way, but also some of the blocks from Brain A. At *a* and surrounded by ink lines is the segment of the section shown under a magnification of 100 diameters in Plate XIV, Fig. 43, and as is here seen is taken from the lateral aspect near the vertex, instead of from the vertex as in the corresponding plate of the normal cortex (Plate VII, Fig. 21). The first layer averages .25 mm. in thickness and contains numerous capillaries with thickened walls, and tortuous course with larger and smaller perivascular spaces. Numerous neuroglia cells are scattered throughout this layer. The second layer is here 1.50 mm. in thickness. Here, too, are seen numerous capillaries with thickened walls, irregular course, and large perivascular spaces. In the upper half of the layer the small pyramidal cells gradually are intermingled with larger pyramidal cells as the lower portions are reached, until just above *a* the largest pyramids of the section are seen singly or in groups in a comparatively narrow zone. Below and opposite *a* is a narrow zone, some .25 mm. in width in which there are practically no large pyramidal cells. Below this again is a very narrow zone at the lower part of this layer in which some few large pyramidal cells are seen scattered among the smaller and irregular cells. These cells present all stages of chromatolysis, pigmentation, shrinkage of the cell-body and processes and irregularity in direction of the latter, eccentricity and shrinkage of the nucleus and larger and smaller pericellular spaces. Numerous neuroglia cells are scattered throughout the layer. The third, or spindle cell layer, measures scarce .50 mm. in thickness and contains for the most part shrunken and irregular spindle cells in larger or smaller pericellular spaces, in many instances in various stages of chromatolysis. Numerous neuroglia cells in many cases appearing in direct contact with the cell-body are seen in this layer, as well as in the above layer. The vascular changes are also similar. The entire depth of the cortex here is thus 2.25 mm., somewhat less than in Plate VII. Fig. 21, but about the same as on the lateral aspect of this latter plate. Nerve and neuroglia cell counts were made here in the same manner as in previous sections, and it was found that there was an average of 68.63 nerve cells and 192.70 neuroglia cells to each square millimeter of surface of the section as compared to 104 nerve cells and 180.90 neuroglia cells in the corresponding region of Brain A, both sections being of the same thickness and stained in the same manner with methylene violet.

Temporal Region.—Turning to the region below this we come to the temporal region represented here by a section from the first temporal convolution near its anterior extremity, from the point *I* in Plate X. Fig. 29, and shown under a magnification of fourteen diameters in Plate XIV. Fig. 44. This convolution is also much narrower than the corresponding convolution of *Brain A,* seen in Plate VIII, Fig. 22, thus having a somewhat dissimilar mechanical arrangement. To the right is seen the first temporal fissure and a portion of the second temporal convolution. The convolution measures 5.5 mm. in width and 8 mm. in depth from

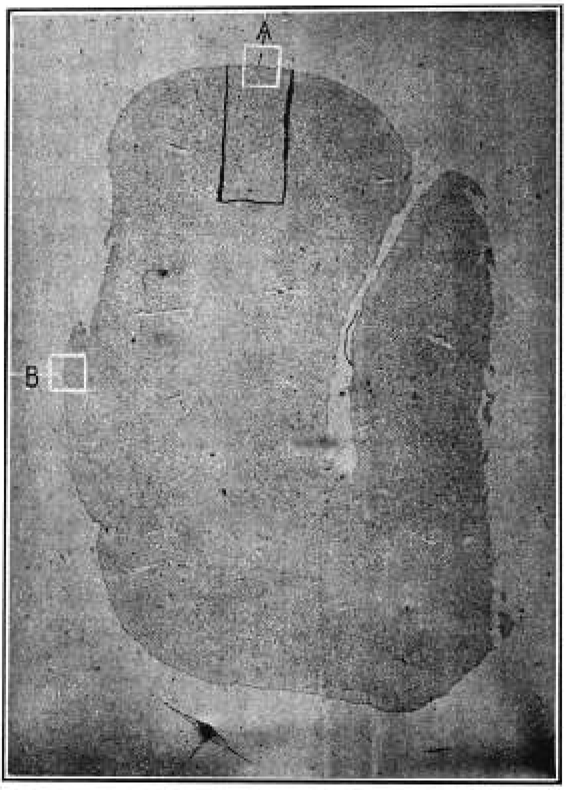

Plate XIV, Fig. 44.

the vertex to the point on the level with the bottom of the first temporal fissure and is 6 2-3 microns in thickness. The convolution at this point is seen on the right to curve around and fuse with the second temporal convolution, being free above at *b*, which is the lower boundary of the fissure of Sylvius at the beginning of the posterior branch. At *a* and enclosed in ink lines is the segment of the section shown in the following plate under a magnification of 100 diameters. The first or superficial layer is quite uniform in thickness, broken in several places, especially above *b* on the superior surface. The second layer shows the striated arrangement of the cells only very indistinctly at some few points and contains many pericellular and perivascular spaces, some with and others without contents. The third layer is indistinct and fades into the white medullary center which is narrow and passes inferiorly over to connect on the right with that of the second temporal convolution.

In Plate XV, Fig. 45, strip *a* of Plate XIV, Fig. 44, under a magnification of 100 diameters, the pathological conditions are seen to be well marked. The section is 6 2-3 microns in thickness and stained with methylene violet. Here the first layer averages about .20 mm. in thickness and to the right a fragment of a blood vessel is seen at the surface, but penetrating the cortex in a different plane. In the center and reaching into the second layer is a large capillary with thickened walls, with larger caliber above and smaller below, being somewhat funnel shaped and surrounded by a large perivascular space. Some smaller fragments of capillaries and neuroglia cells are scattered about in the layer. The second or pyramidal cell layer is 1.50 mm. in thickness and presents very much the same general plan of arrangement as the corresponding region in the normal brain, as seen in Plate VIII, Fig. 23, and also in the region of the first frontal convolution, as seen in Plate II, Fig. 3, and XI, Fig. 31. Small pyramidal cells almost exclusively are seen in the upper part of the layer below this gradually increasing in size to the middle of the layer. Then opposite *a* is a narrow strip some .20 mm. in thickness in which there are small pyramidal cells almost exclusively. Below this again and in the lower part of this layer are larger pyramidal cells, intermingled with smaller pyramidal and irregular shaped cells. Here, too, the majority of the cells are seen shrunken and surrounded by larger and smaller pericellular spaces. Various stages of chromatolysis, shrinkage and eccentricity of the nucleus and atrophy of the cell processes are to be observed. The blood vessels show the same pathological conditions as in the upper layer and numerous neuroglia cells are interspersed thickly everywhere.

The third layer is .80 mm. in thickness and presents the same pathological conditions of the cells and blood vessels as previously described for this layer in Plate XIV, Fig. 43, of the parietal region. The entire depth of the cortex here is 2.50 mm., somewhat thicker than the corresponding region of *Brain A.* Nerve and neuroglia cell counts were also made here and in a similar manner, an average of 56.74 nerve cells and 205.90 neuroglia cells being found to the square millimeter of surface of the cortical portion of this section, as compared to 146. nerve cells and 131.90 neuroglia cells to the square millimeter of the surface of the cortex in the corresponding region of *Brain A.* In the latter methylene blue was the stain used, the thickness of the sections being the same in both cases, and as has been seen in every instance the methylene violet stain has greater affinity for the neuroglia cells than the methylene blue, whereas, the nerve cells stain about the same with the one as with the other.

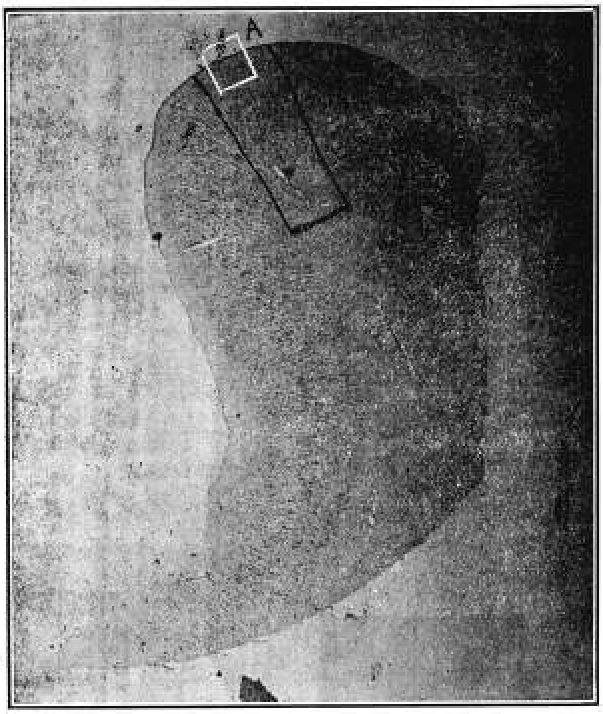

Plate XV, Fig. 46.

Occipital Region.—Plate XV, Fig. 46, is a photomicrograph magnified fourteen diameters of a section taken from the block *J* of Plate X, Fig. 29, situated in the upper portion of the lateral aspect of the occipital convolution. The section is 5 mm. wide, 8 mm. in length and 6 2-3 microns in thickness, was fixed in 95% alcohol, and stained with methylene violet. As may be observed, upon the posterior aspect, the sulcus is very shallow, the cortex here fusing with that of the adjacent gyrus not far from the vertex, whereas anteriorly the sulcus is well marked and quite deep. The first or outer layer is thicker both on the posterior and anterior aspects than at the vertex and is quite uniformly regular in outline. The second layer is well marked and shows the striated arrangement of the cells quite as well as in *Brain A,* at this point. Numerous large cells, some of which quite approach the Betz cells in size and structure, are seen scattered in the middle and lower portions of the layer. The third or spindle cell layer below is gradually lost in the white medullary substance. Throughout the entire section the cells and their arrangement are well made out, the capillaries although having thickened walls and somewhat tortuous are less conspicuous, the pericellular spaces smaller and less numerous, and most of the cells are fairly normal and show no distinct pathological changes. At *a* and enclosed in ink lines is the position of the segment in the adjacent section from which Plate XV, Fig. 47, was taken. This latter corresponds most favorably with Plate IX, Fig. 25, from the corresponding region of the normal brain and some of the nerve cells here in Plate XV, Fig. 47, are larger and more numerous than in the corresponding section from *Brain A.* The first or outer layer is uniform in outline and measures here but .15 mm. in thickness. It contains numerous neuroglia cells and some scattered small nerve cells similar to those described in Plate II, Fig. 3, and seen in the text as Figs. C, D, E, and F. The second or pyramidal cell layer is of special interest and measures 1.40 mm. in thickness, being somewhat deeper than in Plate IX, Fig. 25, but with a similar arrangement of cells. Above are small pyramidal cells only, then larger pyramidal cells are seen in the deeper portions until about the middle of the layer is a region containing very large pyramidal cells, same as the one indicated by the letter X, for instance, being similar in size and structure to the Betz cells. Below this at *a* is a region .30 mm. in thickness in which numerous small pyramidal cells are alone seen. Below this again is a narrow zone containing some larger pyramidal cells scattered amongst the small pyramidal and irregular cells. The cell marked in the plate by the letter X is seen magnified in Fig. X. It is very large, contains irregularly elongated and linear chromophilic bodies of considerable size and arrangement in a more or less parallel direction to the cell-body and extending into the dendritic processes. The nucleus is large, rounded, distinct, and centrally located with a distinct rounded nucleolus and indefinite chromophilic network within. No processes are given off at the base in this plane, but a large process is given off upon the right at the level of the nucleus and soon divides into two branches. Another process is given off to the left on the opposite side of the cell-body at a level just above the nucleus. The apical dendric process contains numerous linear chromophilic bodies extending for some distance into the same. This is a stichochrome nerve cell of the somatochrome class, and, in size and structure, is similar to the Betz cell. The two cells to the extreme right are similar in structure but not as large as the above. There are no pathological changes to be determined in the cells of this layer. Several small capillaries are seen with somewhat thickened walls, indicating that possibly the blood vessel changes are the first to be found in the disease, but of course much more extended observation and study would be required to determine the full relation of all these pathological processes to one another. The third or spindle cell layer is here .90 mm. in thickness and made up of spindle and irregular polygonal cells, quite normal in appearance for the most part; some, however, showing slight shrinkage, pericellular spaces, and slight beginning chromatolysis. Some capillaries with thickened walls and perivascular spaces are to be observed here also. The entire thickness of the cortex measures 2.45 mm. being .45 mm. thicker than in Plate IX, Fig. 25. Nerve and neuroglia cell counts were made here with the results that 62.50 nerve cells and 215.01 neuroglia cells were found on an average to each square millimeter of surface of the cortex here, as compared to 164. nerve cells and 199. neuroglia cells in the same area of the corresponding section of *Brain A*, both sections being 6 2-3 microns in thickness and stained with methylene violet. From a study of the above plates from these two brains, the cortex in *Brain A*, would seem to be thinner and more compact, whereas, the cortex of *Brain B*, on an average measures somewhat thicker, yet the cells seem more scattered, so that a very much higher average of nerve cells is to be found in the former, far more it seems to the writer than could be accounted for by the possible destruction of some of the cells in the sections of *Brain B*, due to pathological agencies.

The careful detailed study of the sections from various parts of the different regions of Brain A, practically normal from a histological standpoint, and of corresponding sections of Brain B, a case of advanced dementia paralytica in the manner as described in this article has led the writer to the following conclusions: I. Photomicrography is a useful and valuable adjunct to such work, giving greater accuracy in relations of parts to one another than is possible in drawings and showing conditions as they actually appear to the eye of the observer in each particular plane when the sections are seen under the microscope. Powers of 14 or 20 diameters show very well relations of the layers to one another, and also the relation of the groups of large cells; such as the Betz cells in the central regions, for instance. Powers of 100 diameters are well adapted to the study of the more minute detail of these relations of the layers and of various cells to one another, and also some of the morphology of the individual cells can be made out. Powers of 1,000 to 1,500 diameters show the internal structure of the cell to excellent advantage, but only in the very limited plane at which the object is focussed. On the other hand, the disadvantage of photomicrography is that everything is shown in any one plane so that special parts or structures are not brought out as prominently as in schematic drawings, and on this account all such work should be accompanied by such drawings to make it more complete. It is furthermore often quite difficult to obtain any one plane showing most of the cell structure, to say nothing of all of the same.

II. Artefacts of many kinds are to be found in such work, and should be carefully avoided and eliminated in every instance before definite conclusions are drawn from any series of observations. Pressure and other mechanical causes acting before death, that due to manipulation at autopsy, artefacts resulting from fixation, imbedding, sectioning, staining, decolorizing, and even mounting, are all possibilities, and are often most difficult to determine in contradistinction to the pathological changes.

III. The method of transporting material by means of small metallic boxes or similarly sized phials, permitting of a free circulation of various kinds of fixative fluids, without injury, and also permitting of subsequent exact localization, the process requiring a minimum of time and space is, to the mind of the writer, of decided practical value in such work. This method is fully described in the text under the heading of "Technique."

IV. Nerve and neuroglia cell counts have been alluded to above, but a few remarks upon method may be of value. The method of counting the same from photomicrographs of moderate magnification is not accurate, as cells may overlap or be arranged in dense groups or their images may not all be sufficiently distinct so as to differentiate them properly, especially does this apply to the neuroglia cells, which are very small and often closely aggregated. Photomicrographs magnified a thousand diameters or more, although showing all the cells visible, are much too limited in area. For these reasons the use of the ocular net-micrometer was found to be the best and most accurate for this work, using a stage micrometer to determine the relation of the ocular field to the actual size of the section. In this way the exact number of nerve and neuroglia cells can be determined for any number of fields and an average obtained for any area, as was done in various plates in the brains employed in this work, as seen in Table II. As will be noted by referring to this latter, there is considerable variability in the number of nerve and neuroglia cells not only in different cortical regions but also from adjacent sections of the same region. The stain is seen to play an important rôle here in the resulting average number of neuroglia cells, methylene violet having a greater affinity for these cells than methylene blue. Sections stained by the latter cannot always be depended upon to show all the neuroglia cells. In comparing the normal paretic brain there is marked diminution of the nerve cells in the latter as compared to the former, whereas the neuroglia cells, making due allowance for variability, are somewhat increased in number in the paretic brain.

V. The thickness of the layers is not constant in different parts of the same gyrus, nor even in different portions of a single transverse section of a gyrus, to say nothing of different regions of the cortex. In the same way there is greater or less variability in the shape and mechanical arrangement of each gyrus in contrast to the other gyri making up the surface of the hemisphere and different parts of the same gyrus vary in this respect. This will be best observed by referring to the several plates of both Brains A and B, magnified 14 diameters, and of the various regions of the cortex.

VI. After a quite extended perusal of the literature upon the structure of the cortex as presented in the first portion of this article, the writer inclines to the view of a three-layered type of cell arrangement in the cortex, as the type with, of course, variations in special parts, as the cornu ammonis, for instance. This is shown in Table I, and brief is as follows: 1, or superficial layer, containing but few nerve cells, many neuroglia cells, and many chiefly tangential fibers. The first two elements only are seen with the Nissl stain, whereas the latter element is most conspicuous with Weigert's stain, and for this latter reason Ramon y Cajal designated it as the tangential fiber layer; 2, or pyramidal cell layer, to reduce the layering of the cortex to its lowest terms, and including the small, large, and giant or Betz pyramidal cells all in this one layer; 3, or spindle cell layer, including both the spindle cells which are in the majority and the less numerous irregular polygonal cells. Below these three layers is the sub-cortical white medullary substance.

VII. The study of the internal structure of the normal brain from a histological standpoint (Brain A) by the Nissl method shows four principal types of nerve cells: (1) The small rounded nerve cells of the first layer with or without one or more dendritic processes—rarely more than two, containing a rounded nucleus almost filling the body of the cell, this latter surrounded by a partial or complete narrow band of finely granular chromophilic substance. The neucleus contains a well marked neucleolus and slightly stained protoplasmic substance. These are co-called karyochrome nerve cells of Nissl's classification. (2) The pyramidal cells of the second layer, of which there are four varieties (a) the small pyramidal cells, (b) the large pyramidal cells, (c) cells intermediate in size and structure between the large pyramidal cells and the typical giant pyramidal or "Betz" cells, and (d) the giant pyramidal or "Betz" cells. In the smaller pyramidal cells it is difficult to distinguish distinct chromophilic granules, but the chromatin is arranged in larger or smaller finely granular masses in various parts of the cell-body, sometimes aggregated about the nucleus, at other times near the base or dendritic processes. The larger pyramidal cells, however, have the increasing amount of chromatic substance arranged in more or less distinct larger and smaller chromophilic granules, and these arranged in a direction parallel to the surface of the cell-body. Still larger in size and more distinct in the arrangement of chromophilic granules in this general parallel manner are the intermediate variety of these pyramidal cells, which, although larger than the average pyramidal cell are considerably smaller than the typical Betz cell, and have a wider range of distribution not only in the vertical extent of the second layer of the cortex, but also in the different regions of the cortex, being found in the central, parietal, temporal, and occipital regions. Finally the largest in size and most distinct in structure, especially in the arrangement of the chromatic substance, are the giant pyramidal or Betz cells, in which larger size, large distinct nucleus and nucleolus, and also large parallel arranged chromophilic granules are seen in the cell-body, and often extending far up into the dendritic processes. These are localized, for the most part, in the lower portion of the second layer in certain areas of the central convolution and the posterior portion of the superior frontal convolutions. These pyramidal cells as a whole can best be designated as stichochrome nerve cells of the somatochrome class in Nissl's classification, although the smaller pyramidal cells may simulate more the gryochrome nerve cells of this same class, owing to the indistinct arrangement of the chromatic substance. (3) The spindle cells found in the third layer and containing a very large nucleus with well marked nucleolus. The nucleus is often so large that it seems disproportionate to the size of the latter. The chromatic substance here is finely granular and arranged in irregular masses or heaps about the nucleus, and extending into the base of the dendritic processes, these latter, usually two in number and opposite, producing a bipolar condition. These cells are gryochrome nerve cells of the somatochrome class. (4) Finally irregular or polygonal nerve cells are found in the second and third layers. These cells are irregular in shape, with three or more dendritic processes, a large nucleus containing a well marked nucleolus. In the cell-body are irregular finely granular masses of chromatic substance similar to the spindle cells in this respect, so could fall in the same classification as gryochrome nerve cells of the somatochrome class. In the cerebellum, the Purkinje cells, with their chromatic substance more or less arranged in a network, are classified as arkychrome nerve cells of the somatochrome class, whereas the small nerve cells of the granular layer, with small nucleus, appear only partially surrounded by the cell-body, are classified as cytochrome nerve cells. The four types of cells above mentioned, as found in the cerebral cortex, were seen in all the regions of the external surface of the hemisphere studied. In addition to these cellular elements of the nervous tissue the neuroglia cells of the interstitial tissue were everywhere to be seen, and in the walls of the blood vessels the vascular cellular elements were also to be found.

VIII. Previous investigators, in the study of the cerebral cortex in dementia paralytica by the use of the Nissl method, have noted the following pathological changes: Various stages of cell degeneration up to complete destruction of the same, consisting of diminution, disintegration, and vacuolization of the cell protoplasm, all stages of chromatolysis up to complete disappearance of the chromatic substance, shrinkage with deformity of the contour of the cell-body, atrophy of the dendritic processes, various degrees of pigmentation and pigmentary deposits in the cell-body, also adjacent to blood vessels; shrinkage with diminution in size, irregularity, compression, vacuolization, and eccentricity of the nucleus with even extrusion of the same from the cell-body by the rupture of the cell wall, or complete sclerosis of the nucleus with homogeneous and tinged contents or crystalline deposits, nucleolus displaced to nuclear wall or indistinguishable or vacuolated, calcareous deposits in the form of fine granules, crumbs, placques, or stalactitic masses intensely colored with methylene blue and found in the bodies of the sclerosed cells, part or whole of cell entirely bleached, complete necrosis of cells, reduction in number of nerve cells, thickening of pia with septa projecting into the cortex, granular crowding of variously stained granules, obscure layering of the cortex, multiplication of white corpuscles, proliferation of neuroglia cells, increase in and dilatation of capillaries and arterioles, with thickening of walls of same by encasement of latter with lymphatic corpuscles, and finally proliferation of interstitial network. The writer has observed all of these changes excepting the following: vacuolization of the cell protoplasm was not observed in the paretic material examined in this work, no pigmentary deposits were observed outside of the nerve cell bodies, although varying amounts were found in many of the nerve cells. No vacuolization of the nucleus or extrusion of the same was found here, no crystalline or calcareous deposits were made out in any of the cells, no septa were observed penetrating from the thickened pia into the cortex, multiplication of white corpuscles was not observed, and proliferation of neuroglia cells as seen from the nerve and neuroglia cell counts as tabulated in Table II. seems to have existed to but a slight extent in small localized places, as about some of the necrosed nerve cells. The writer does not mean to say that this may not occur in some cases, for on the contrary he is inclined to think it may occur under certain conditions, either localized or more general. Also no proliferation of the interstitial network was observed here. About the nerve cells pericellular spaces of greater or less extent were observed in many cases. In some only a small portion of the cell-body, or a single dendritic process, was surrounded by a limited space; in many, however, a large portion of all the cell-body was thus surrounded. Perivascular spaces were also observed of varying size and extent about many of the blood vessels of the cortex. Pigmentation, in addition to being present in many of the nerve cells of the first and second layers of the cortex in the central regions, was also observed in cells of these layers in the frontal region as well; also in the parietal and temporal regions, but not in the occipital region. The pathological process here was most severe in the central and frontal regions, extending to a lesser extent, but still very marked, into the temporal and parietal regions, whereas the occipital region almost entirely escaped and appears practically normal. In the regions involved in this case the disease seems to be a chronic disease of the nerve cells with pigmentary degeneration and a necrosis of the cell-body, partial or complete, with accompanying involvement of the blood vessels. The relation of the vascular and cell changes to one another and the order of procedure in time is one that the writer believes requires much more extended investigation before it can be answered satisfactorily.

In conclusion the writer gratefully acknowledges the kindly interest, suggestions, and assistance offered by Professor H. Fairfield Osborn, Dr. Oliver S. Strong, and Dr. Edward Leeming, of Columbia University; Dr. Ira Van Giesen, former Director of the

New York State Pathological Institute; Dr. H. T. Brooks, Professor of Histology and Pathology at the New York Post-Graduate Medical School, and Hospital; Dr. Philip F. O'Hanlon, Coroner's Physician, New York City, and Dr. Robert T. Irvine, of Ossining, N. Y.

LITERATURE.

Anglade, D. "Sur les alterationes des cellules nerveuses de la cellule pyramidale in particular dans la paralysie générale." Annales Medico-Psychologiques. Huitiéme Série, Tome Huitiéme, Sinquante sixieme Anneé (1898), p. 40.

Arndt, R. "Untersuchungen über die ganglion-Körper des Nerves sympathicus." Arch. f. mikr. Anat. Bonn. Bd. X. (1874), S. 208-241.

Baillarger, J. "Recherches sur la structur de la couche corticale des circonvolutions du cerveau." (1840). Annales Med.-Psychol. (1855). I., 1-3. "De l'idiotie." Gaz. des hôp. (1855). No. 84 Canst. Jahresber. (1855). III., p. 8, Mem. de l'Acad. de Med., (1880). VIII. Bull. de l'Acad. de Med. (1856, Juillet). Gaz. habdom. (1859). (Cit. Griesinger, p. 366). Acad. de Med. (Cit. Griesinger, p. 360). Annal Med.-Psychol., 1882, VII. 1, p. 19. Baillarger et Gratiolet. Acad. de Méd. (May 26, 1857) (Cit. Griesinger).

Ballet, Gilbert. "Les Lesions cérébrales de la paralysie générale étudiées par la méthode de Nissl." Ann. Méd. psychol. Par. 8. s. t. VII (1898), pp. 448-459.

Barker, L. T. "The Nervous System and Its Constituent Neurones." D. Appleton & Co., N. Y., 1899.

Belmondo, F. "Alterazione dei centri nervosi nella paralisi progressiva." Annali di Neurolgia (1896). p. 475.

Berger, H. "Degeneration du Vorderhornzellen des Ruckenmarks bei Dementia paralytica." Monatschrift f. Psych. u. Neur. (1898), H. I.

Berlin, R. "Beiträge sur Structurlehre d. Grosshirnwindungen." Erlanger (1858).

Benda, C. "Ueber die Bedeutung der durch basiche Anilinfarben darstellbaren Nervenzellstructuren." Neurol. Centralbl. Leipz. Bd. XIV, (1895), S. 759-768.

Betz, W. "Ueber die feinen Structur d. Menschl. Gehirnrinde." Med. Centralbl. (1881). Centralbl. f. d. Med. Wissensch. (1881). N. r. 11-13. Centralbl. f. d. Med. Wissensch. (1874). N. 37-38.

Boedecker and Juliusberger. "Anatomische Befunde bei Dementia paralytica." Neur. Cent. (1897), p. 774.

Boll, F. "Die Histiologie und Histiogenese der nervösen Centralorgane." Archiv. f. Psych. (1873), IV, pp. 1-38.

Cajal, S. Ramón y. "Les nouvelles idées sur la Structure du système nerveux chez l'homme et chez les vertébrés." (1895.)

Charcot, J. M. "Anatomie Pathologique." Le Progres Médical, p. 253 (1871).

Clarke, L. "Notes on Researches on the Intimate Structure of the Brain." Proc. Royal Society of London, Vol. XII, p. 716 (1863).

Cleland, John. "Human Anatomy, General and Descriptive." p. 627 (1876).

Crisafulli, E. "Studio comparativo clinico istologico sulla paralisi generale progressiva." Ann. di Neurolog. 14, p. 255. Also: Ulteriore contributo alla istologia path. della paralisi generale progressiva." Annali di Neurolog. (1897), p. 194.

De Quervain, Fritz. "Ueber die Veränderungen des Central nervensystems bei experimentellen Kachexia thyreoidea der Thiere." Arch. f. path. Anat. etc., Berl. Bd. CXXXIII (1893), S. 481.

Dogiel, A. S. "Zur Frage über den Bau der Nervenzellen und über des Verhältniss ihres Achencylinder (Nerven) Fortsätzes zu den Protoplasmsfortsätzen (Dendriton)." Arch. f. mikr. Anat., Bonn. Bd. XLI (1893), S. 62-87. Also: "Zur Frage über des Verhalten der Nervenzellen zu einander. Arch. f. Anat. u. Physiol. Anat. Abth. Leipz. (1893), S. 429-434.

Donaldson, H. H. "The Size of Several Cranial Nerves in Man as Indicated by the Areas of their Cross-sections." Amer. Jour. of Psychol., 4, 1891-1892, p. 227.

Edinger, L. "Anatomy of the Central Nervous System in Man and in Vertebrates in General." (1896.)

Ewing, James T. "Studies on Ganglion Cells." Archiv. of Neurol. and Psychopath., Vol. I, No. 3 (1898).

Flemming, W. "Beiträge zur Anat. u. Embryol. als Festgabe fur J. Henle," (1882), Bonn. S. 12.

Cf. also, "Ueber den Bau der Spinalganglienzellen bei Saugethieren, und Bemerkungen über den centrallen Zellen." Arch. f. mikr. Anat., Bonn. 1895. Bd. XLVI, S. 379-394, and, "Die Struktur der Spinalganglienzellen bei Saugetieren. Arch. f. Psychiat. u. Nervenkr., Berl. Bd. XXIX (1897), H. 3. S. 969-974.

"Ueber die Struktur centrallen Nervenzellen bei Wirbeltieren." Anat. Hefte, I. Abth., 19. Heft. (1896) (Bd. VI, H. 19, p. 561).

Flesch, M. "Ueber Verschiedenheiten im chemischen Verhalten der Nervenzellen." Mitth. d. Naturf. Gesellsch. in Bern (1897) M. 1169-1194, S. 192-199. Bern. P. Haller (1888).

Gennari, Francisco. "De peculiaris structura cerebri, non-nulisque ejus morbis. Pancae aliae anatom. observat. accedunt." XVI, pp. 87, 4re. "Pannae ex regis typg." (1782.)

Golgi, C. "Sulla fina Anatomia Organi Centrali del Sistema Nervosa." (1885.) p. 65. Archiv. ital. de Biol. (1883.) Ref.

Gowers, W. R. "Diseases of the Nervous System." Vol. II, p. 10 (1893).

Hammdrberg, Carl. "Studien über Klinik und Pathologie die Idiotie nebst Untersuchungen über die Normale Anatomie der Hirnrinde." (1895.)

Henle, J. "Anatomie," 2nd Ed. Vol. II, p. 306 (1876).

Jelliffe, Smith Ely. "Biographical Contribution to the Cytology of the Nerve Cell." Arch. of Neurology and Psychopathology. Vol. I, No. 3 (1898), p. 441.

Key, E. A. H., and Retzius, G. "Studien in der Anatomie des Nervensystems und des Bindegewebes." 4to. Stockholm (1876).

Kolliker, A. "Mikroskopische Anatomie." Band II (1830). "Handbuch der Gewebelehre." Leipzig (1867).

Krause, W. "Anatomie." Vol. I, p. 439 (1876).

Lewis, Bevan. "Comparative Structure of the Cortex Cerebri." Med. Times and Gaz. (1876, Mar. 4). Brain (1868), Vol. I. Philosophy. Transact. (1880). Lewis and Clarke. "On the Cortical Lamination of the Motor Area of the Brain." Proc. of the Royal Soc. of London (1878). Vol. 27, p. 38.

Luys, J. "Systéme Nerveux," p. 162 (1864).

Major, H. C. "The Histology of the Island of Reil." West Riding Lunatic Asylum Medical Reports. Vol. VI (1876), p. 5.

Meckel, J. F. "Anatomie." Vol. II, p. 443.

Meynert, T. "Der Bau der Grosshirnrinde und seine örtlichen Verschiedenheiten nebst einem pathol. anat." Vierteljahrschr. f. Psychiatrie von Leidesdorf und Meynert (1867), u. (1868). "Corallium," Leipzig (1872), und Stricker's Handbuch (1871). Allg. Wiener med. Ztg. (1868), XIII, Psychiatry, translated by Sachs, B. (1885).

Nagy, A. "An agyking idigsijtjunek elvátozásàról elmebautalmaknâe." Maggae Arvosi Archivum (1894).

"Ueber die Veränderurgen der Hirnrindenzellen bei Psychosen." Neur. Cent. (1894), p. 820.

Nissl, Franz. (a) "Ueber die Untersuchungsmethoden der gross hirnrinde." Tagebl. d. 58, Versamml. Deutsch. naturf. u. aerzte in Strassburg (1885), S. 506.'

Tagebl. de 61 Versamml. Deutsch. naturf. u. aerzte in Koln (1888). Inter. Klin. Rundschau. II (1888). No. 43.

(c) "Die Kern d. Thalamus beim Kaninchen." Tagebl. d. Naturforsch. v. z. Heidelberg (1890), S. 509.

(d) "Ueber die Veränderungen der Ganglienzellen in Facialis Kern des Kaninchens nach ausreissung der Nerven." Allg. Ztschrift. f. Psych. Bd. XLVIII (1891-92), S. 197.

(e) "Ueber experimentell erzeugte Verànderungen an den Verderhornzellen des Rückenmarkes bei Kaninchen mit Demonstration mikroskopische Präparate." Allg. Ztschr. f. Psychiat. Bd. XLVIII (1891-92), S. 675-682.

(f) "Mittheilungen zur Anatomie der Nervenzelle." Allg. Ztschrft. f. Psychiatrie. Bd. L. (1894), S. 370.

(g) "Ueber Rosin's neue Farbemethode des gesammten Nervensystems und dessen Bemerkungen über Ganglienzellen." Neurolog. Centralblatt., XIII (1894), S. 96-141.

(h) "Ueber eine neue Untersuchungsmethode des Centralorganes speziell zur Feststellung der Localization des Nervenzellen. Neur. Centralbl. (1894), S. 507-508. Centralbl. f. Nervenh. K. und Psychiatrie, Bd. XVII (1894, S. 337-344. Arch. f. Psychiat., Bd. XXVI (1894), S. 597-612.

(i) "Ueber die sogenannte Granula der Nervenzellen." Neurologisches Centralblatt., Bd. XIII (1894), S. 676, 781, 810.

(j) "Mittheilungen über Karyokinese in Centralen Nervensystem." Allg. Ztsch. f. Psych., Bd. LI (1894), S. 245.

(k) "Bernhard von Gudden's hirnanatomische experimentale Untersuchungen." Allg. Ztschr. f. Psychiat., Bd. LI (1894), S. 527-549.

(l) "Der gegenwartige Stand der Nervenzellen Anatomie und Pathologie." Centr. f. Nervenheilk. und Psychiatrie, Bd. XVIII (1895). Allg. Ztsch. f. Psych. (1895), p. 981.

(m) "Ueber die Nomenclatur in der nervenzellenanatomie und ihre nächsten Ziele." Neurolog. Centralblatt., Bd. XIV (1895), S. 96-104.

(n) "Mittheilungen zur pathologischen Anatomie der Dementia paralytica." Arch. f. Psychiatrie, Bd. XXVIII (1896), S. 987-992.

(o) "Ueber die Veränderungen der Nervenzellen nach experimentell erzeugter Vergiftung, Neurolog. Centralblatt, Bd. XV. (1896), S. 9.

(p) "Die Beziehungen des Nervenzellensubstanzen zu dem thätigen ruhenden, und ermüdeten Zellzustanden." Neurolog. Centralblatt (1896). Allg. Ztschr. f. Psychiat. (1896), Bd. LII S. 1147.

(q) "Die Hypothese der Specifischen Nervenzellenfunction." Allg. Ztschrft. f. Psych. Berl. Bd. LIV (1897), S. 1-107.

(r) "Ueber die örtlichen Bau verscheidenheiten die Hirnrinde." Arch. f. Psychiat., Bd. XXIX (1897), S. 1025-1027.

(s) "Ueber Nervenzellen und graue Substanz." München med. Woch., Bd. XLV (1898), S. 988; 1023; 1060.

Obersteiner, H. "Central Nervous Organs, Anatomy of in Health and Disease," p. 350 (1887).

Popoff, N. M. "Pathologische anatomische Veränderungen des Centralnervensystems bei der asiatischen Cholera." Virchow's Archiv., 1894, p. 57.

Ranvier, L. "Leçons sur l'histologie du système nerveux." Paris, 1878.

Remak, R. "Anatomische Beobachtungen über das Gehirn, das Rückenmark, und die Nervenwurzeln." Muller's Archiv. f. Anat. und Phy. (1841.)

Neurologische Erlautungen. Arch. f. Anat., Physiol., u. wissensch. Med. Bul., 1844, S. 463-472.

Rosin, H. "Ein Beitrag zur Lehre vom Bau der Ganglienzellen. Deutsche med. Wochenschr. Leipz. u. Berl., Bd. XXII (1896), S. 495-497.

Schaffer, K. "Kurze Anmerkung über die morphologische Differenz des Axencylinders in Verhältnisse zu den protoplasmatischen Fortsätzen bei Nissl's Färbung." Neurol. Centralbl., Leipz., Bd. XII (1893), S. 489-857.

Schultz, Max, in Striker's, S. A. "Manual of Histology." Am. translation. 8vo., N. Y., 1872, p. 134, et seq.

Schwalbe, G. "Lehrbuch der Anatomie des Menschen," arranged by Dr. August Rauber (1885), p. 463. Fig. 279.

Starr, Leaming and Strong. "Atlas of Nerve Cells," p. 72. Fig. 10 (1896).

Vicq d'Azyr, Felix. "Traité d'anatomie et de physiologie." VI. "Anatomie et physiologie du cerveau," 123, 117 pp., 35 pl. (1786.)

Von Lenhossék, M. "Der feinere Bau des Nervensystems im Lichte neuesten Forschungen." 2te Aufl., Berlin (1895).

"Ueber Nervenzellenstructuren." Vorhandl. d. Anat. genellsch., Jena (1896), Bd. X, S. 15-21.

EXPLANATION OF PLATES.

Plate I. Fig. 1. Brain A. Left hemisphere. Electrocuted case, normal histologically.

dicated by the figure 1 in Plate I. Fig. 1. Section 6 2-3 microns in thick-

dicated by the figure 1 in Plate I. Fig .1. Section 6 2-3 microns in thickness stained with methylene blue and magnified 14 diameters.

Plate II. Fig. 3. Brain A. First frontal conv. Strip *a* of Plate I, Fig. 2, magnified 100 diameters.

Plate II. Fig. 4. Brain A. First frontal conv. Cell *G*. of Plate II, Fig. 3 magnified 1400 diameters.

Plate II. Fig. 5. Brain A. First frontal conv. Cell *H* of Plate II, Fig. 3 magnified 1,400 diameters.

Plate III. Fig. 6. Brain A. First frontal conv. Group of spindle cells *I* of third layer of cortex shown at *I* in Plate II, Fig. 3 magnified 1,400 diameters.

Plate III. Fig. 7. Brain A. Ant. cent, conv. Upper third, taken from point indicated by the figure 2 in Plate I., Fig. 1. Section 10 microns in thickness stained with methylene violet, and magnified 14 diameters.

Plate III. Fig. 8. Brain A. Ant. cent. conv. Upper third. Strip *a* of Plate III, Fig. 7 magnified 100 diameters.

Plate IV. Fig. 9. Brain A. Ant. cent. conv. Upper third. Section

from same block and adjacent to that shown in Plate III, Fig. 7. Section 10 microns in thickness, stained with methylene blue, and magnified 14 diameters.

Plate IV. Fig. 10. Brain A. Ant. cent. conv. Upper third. Strip *a* of Plate IV, Fig. 9, magnified 100 diameters.

Plate IV. Fig. 11. Brain A. Ant. cent. conv. Upper third. Section taken from same block and adjacent to that shown in Plate IV, Fig. 9. Section 10 microns in thickness, stained with methylene blue, and magnified 14 diameters.

Plate IV. Fig. 12. Ant. cent. conv. Upper third. Giant pyramidal cell from lower portion of second layer of cortex from section adjacent to that shown in Plate III, Fig. 7. Section 10 microns in thickness, stained with methylene violet and magnified 1,400 diameters.

Plate V. Fig. 13. Brain A. Ant. cent. conv. Upper third. Portion *a* of Plate IV, Fig. 11, magnified 825 diameters.

Plate V. Fig. 14. Brain A. Ant. cent. conv. Upper third. Two giant pyramidal cells from lower portion of second layer of cortex from section adjacent to that shown in Plate IV, Fig. 9. Section 10 microns in thickness, stained with methylene blue and magnified 1,400 diameters.

Plate V. Fig. 15. Giant pyramidal cell from Ant. cent. conv. Upper third, lower part of second layer from approximately the same region as the cells shown in Plate V, Fig. 14, and stained with methylene blue, Section 10 microns in thickness, and magnified 1,400 diameters.

Plate VI. Fig. 16. Brain A. Ant. cent. conv. Lower third, taken from point indicated by the figure 4 in Plate I, Fig. 1. Section 10 microns in thickness, stained with methylene violet, and magnified 10 diameters.

Plate VI. Fig. 17. Brain A. Ant. cent. conv. Lower third. Strip *a* of Plate VI, Fig. 16, magnified 100 diameters.

Plate VI. Fig. 18. Brain A. Post. cent. conv. Middle third. Section taken from the point indicated by the figure 5 in Plate I, Fig. 1. Section 6 2-3 microns in thickness, stained with methylene blue, and magnified 10 diameters.

Plate VII. Fig. 19. Brain A. Post. cent. conv. Middle third, upper portion. Strip *a* of Plate VI, Fig. 18, magnified 100 diameters showing first and second layers and upper portion only of third layer.

Plate VII. Fig. 20. Brain A. Supra-marginal conv. of parietal region taken from point indicated by the figure 7 in Plate I, Fig. 1. Section 6 2-3 microns in thickness, stained with methylene violet, and magnified 14 diameters.

Plate VII. Fig. 21. Brain A. Supra-marginal conv. of parietal region. Strip *a* of Plate VII, Fig. 20, magnified 100 diameters.

Plate VIII. Fig. 22. Brain A. First temp. conv. taken from point indicated by the figure 6 in Plate I, Fig. 1. Section 6 2-3 microns in thickness, stained with methylene blue, and magnified 14 diameters.

Plate VIII. Fig. 23. Brain A. First temp. conv. Strip *a* of Plate VIII, Fig. 22, magnified 100 diameters.

Plate VIII. Fig. 24. Brain A. Occipital conv. taken from point indicated by the figure 8 in Plate I, Fig. 1. Section 6 2-3 microns in thickness, stained with methylene violet and magnified 14 diameters.

Plate IX. Fig. 25. Brain A. Occipital conv. Strip *a* of Plate VIII, Fig. 24, magnified 100 diameters.

Plate IX. Fig. 26. Brain A. Large pyramidal cells from layer of large pyramidal cells of the hippocampus major or cornu ammonis. Section 6 2-3 microns in thickness, stained with methylene violet, and magnified 1,400 diameters.

Plate IX. Fig. 27. Brain A. Purkinje and granular cells from cortex

of left cerebellar hemisphere. External surface. Section 10 microns in thickness, stained with methylene blue, and magnified 1,400 diameters.

Plate X. Fig. 28. Brain A. Multipolar ganglion cell from ant. horn of lumbar enlargement of spinal cord. Section 6 2-3 microns in thickness, stained with methylene violet, and magnified 1,400 diameters.

Plate X. Fig. 29. Brain B. Left hemisphere. Case of dementia paralytica dying in advanced stage of terminal dementia with contractions. Normal size.

Plate X. Fig. 30. Brain B. First frontal conv. taken from point indicated by letter *K* in Plate X, Fig. 29. Section 10 microns in thickness, stained with methylene blue, and magnified 14 diameters.

Plate XI. Fig. 31. Brain B. First frontal conv. Strip *a* of section adjacent to that shown in Plate X, Fig. 30, 6 2-3 microns in thickness, stained with methylene blue, and magnified 100 diameters.

Plate XI, Fig. 32. Brain B. Ant. cent. conv. Upper third taken from point indicated by letter *D* in Plate X, Fig. 29. Section 10 microns in thickness, stained with methylene violet, and magnified 14 diameters.

Plate XI. Fig. 33. Brain B. Ant. cent. conv. Upper third. Strip *a* of section adjacent to that shown in Plate XI, Fig. 32. Section 6 2-3 microns in thickness, stained with methylene violet, and magnified 100 diameters.

Plate XI. Fig. 34. Brain A. Ant. cent. conv. Upper third taken from point indicated by letter *L* in Plate X, Fig. 29. Section 6 2-3 microns in thickness, stained with methylene violet, and magnified 14 diameters.

Plate XII. Fig. 35. Brain B. Ant. cent. conv. Upper third. Giant pyramidal cell *a* of Plate XI, Fig. 34, magnified 1,400 diameters.

Plate XII. Fig. 36. Brain B. Ant. cent. conv. Upper third. Giant pyramidal cell *b* of Plate XI, Fig. 34, magnified 1,400 diameters.

Plate XII. Fig. 37. Brain B. Ant. cent. conv. Upper third. Giant pyramidal cell from section adjacent to that shown in Plate XI, Fig. 34, magnified 1,400 diameters.

Plate XII, Fig. 38. Brain B. Ant. cent. conv. Upper third. Giant pyramidal cell from same section as that from which Plate XII, Fig. 37, was taken, magnified 1,400 diameters. Shows advanced chromatolysis.

Plate XIII. Fig. 39. Brain B. Ant. cent. conv. Upper third taken from point indicated by letter *O* in Plate X, Fig. 29. Section is 10 microns in thickness, stained with methylene violet, and magnified 15 diameters.

Plate XIII. Fig. 40. Brain B. Post. cent. conv. Middle third taken from region indicated by letter *B* in Plate X, Fig. 29. Section is 6 2-3 microns in thickness, stained with methylene blue, and magnified 14 diameters.

Plate XIII. Fig. 41. Brain B. Post. cent. conv. Middle third. Strip *a* of Plate XIII, Fig. 40, showing first and second layers of cortex and upper part of third layer, magnified 100 diameters.

Plate XIV. Fig. 42. Brain B. Supra-marginal conv. of parietal region taken from point indicated by letter *H* in Plate X, Fig. 29. Section 6 2-3 microns in thickness, stained with methylene violet, and magnified 14 diameters.

Plate XIV. Fig. 43. Brain B. Supra-marginal conv. of parietal region. Strip *a* of Plate XIV, Fig. 42, magnified 100 diameters.

Plate XIV. Fig. 44. Brain B. First temp. conv. taken from region indicated by letter *I* in Plate X, Fig. 29. Section 6 2-3 microns in thickness, stained with methylene violet, and magnified 14 diameters.

Plate XV. Fig. 45. Brain B. First temp. conv. Strip *a* of Plate XIV, Fig. 44, and magnified 100 diameters.

Plate XV, Fig. 46. Brain B. Occipital conv. taken from point indicated by letter *J* in Plate X, Fig. 29. Section 6 2-3 microns in thickness, stained with methylene violet and magnified 14 diameters.

Plate XV. Fig. 47. Brain B. Occipital conv. Strip *a* of Plate XV, Fig. 46, magnified 100 diameters.